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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

McDERMOTT, W., DEUSCHLE, K., ADAIR, J., FULMER, H. & LOUGHLIN, Bernice. **Introducing Modern Medicine in a Navajo Community. Physicians and Anthropologists are cooperating in this Study of Changing Patterns of Culture and Disease.** *Science.* 1960, Jan. 22 & 29, v. 131, 197–205; 280–87, 14 figs. [18 refs.]

Technological development in medicine as in other disciplines has "great potential for either good or harm", and interests both the social and the medical scientist. The effect of the impact of such development on people who have as yet been little affected by economic advance was thought to be a desirable field of study, and the opportunity arose when congressional action made the U.S. Public Health Service responsible for the health of Indians in the United States. Negotiations were opened with the Navajo Tribe, comprising 85,000 persons living on their own ancestral land in Arizona, Utah and New Mexico, and this important survey was begun.

The authors describe the Navajo style of life in which farming, weaving and other domestic industries are associated with outside employment on the railroad or in harvesting crops. Sanitation hardly exists, and the conditions and type of life—the tribal desires and expectations and culture, as well as terrain—resemble the conditions existing in many parts of Asia, Africa and South America.

Demographic study indicated an average birth rate of 48·7 per 1,000, a death rate of 7·3 and an infant mortality rate of 73·1. But a warning is given that facts relating to births and deaths were difficult to obtain. An attempt was made to examine every member of the community with whom the staff had any medical relationship, and it was found that three-quarters of the disease was microbial in origin, tuberculosis accounting for 9% though the incidence was falling. Pneumonia, infant diarrhoea, measles and streptococcal infections were prominent, and also trachoma. A common disability was congenital dislocation of the hip, and this was hardly regarded seriously by the Indians. There is probably a hereditary element in it, but it is possible that the habit of lacing infants on to cradle boards, with outstretched legs in a position which does not favour continued insertion of the head of the femur into the pelvic joint, may be a factor. Surgical fusion of the joint is not acceptable because the child would not then be able to sit on the ground with the rest of the family at mealtimes, and would not be able to ride a horse. This is a significant condition which illustrates the concept that health "is a relative matter and signifies the degree to which a person can operate effectively within the particular circumstances of his heredity *and environment*".

The disease pattern is one of high infant mortality and premature death, largely from microbial diseases, and by the time a child arrives at school aged 5–6 years, much of which is to happen has already happened; "a program of *preventive* medicine, to be fully effective, must be inaugurated with the pre-school children".

Health visitors are important, and one person should undertake all sides of the work. One of the difficulties is to ensure that a programme of drug taking on an out-patient basis is properly carried out. Another is to translate Navajo concepts of disease into the English language, and *vice versa.* Medicine men are powerful; they are not only healers, but are spiritual leaders, and they distinguish between illness most likely to respond to their own traditional practices, and illness most likely to respond to western medicine. They raise no objection to western medicine.

In developing programmes of health reform the authors think that the "question of pace looms importantly"; they have not solved it, and they think that a wrong tempo may do real harm. They quote KENNAN (*Realities of American Foreign Policy*, Princeton, N. J., 1954, Princeton Univ. Press):—

" Wherever the authority of the past is too suddenly and too drastically undermined—wherever the past ceases to be the great and reliable reference book of human problems—wherever, above all, the experience of the father becomes irrelevant to the trials and searchings of the son—there the foundations of man's inner health and stability begin to crumble. Insecurity and panic begin to take over, conduct becomes erratic and aggressive. These, unfortunately, are the marks of an era of rapid technological or social changes. A great portion of our globe is today thus affected. And if the price of adjustment to rapid population growth is to cut man's ties to the past and to catapult him violently across centuries of adjustment into some new and unfamiliar technological stratosphere, then I am not sure that the achievement is worth the price."

Charles Wilcocks

SHANNON, H. **Social Influences in Health and Disease.** *Med. J. Australia.* 1960, Feb. 6, v. 1, No. 6, 202–6, 11 figs.

This is a version of the opening paper read at a residential seminar in Melbourne in 1959 for principals of teachers' colleges, educational psychologists, physical educationists and school medical officers. The speaker described some of the remarkable improvements in the state of the public health which have occurred in the last half-century and discussed the factors—environmental, social and educational—which have played their part in bringing about these improvements. Among the diseases the incidences of which were considered are typhoid fever and tuberculosis, and infant mortality. Nevertheless, in spite of the lessening of disease and the betterment of general health, many problems remain such as the different experience of disease in the 5 social classes of the Registrar General, the increasing mortality from respiratory cancer, the high proportion of accidents particularly in children and the rising incidence of coronary disease. The view sustained in this paper is " that the future of preventive medicine will be different from the past, and that the most powerful instrument in effecting its aims will be health education ". *M. E. Delafield*

FRANCIS, T., Jr. **Research in Preventive Medicine.** *J. Amer. Med. Ass.* 1960, Mar. 5, v. 172, No. 10, 993–9.

This paper which comes from the Department o Epidemiology and Virus Laboratory, School of Publi Health, University of Michigan, was read at a meetin of the American College of Preventive Medicine hel in 1959 in Atlantic City, New Jersey.

The author discussed the concept of health an " positive health ", in terms of conditions of moder civilized life. Although descriptive information o diseases " has increased tremendously . . . we hav gained only a slight foothold in understanding th mechanisms involved in disease processes ". Further more " we have no adequate body of measurements o health " and the " so-called health statistics are com monly disease or death statistics ".

The areas of true prevention now available ar summarized as (1) protection from chemical an physical exposure particularly in the field of occupa tional health, (2) prevention by correction of dietar deficiency or excess, and (3) prevention of infectiou disease by specific measures and sanitary social pro cedures. In connexion with the last of these it i pointed out that the " commonly repeated assuranc that infectious disease is conquered is simply not i keeping with the evidence ". Among quotations of thi evidence it is reported by the United States Nationa Health Survey that in 1957–8 with a total of " 76- million days of bed disability caused by all chroni conditions in the United States in one year, there wer 593 million from acute respiratory disease alone ".

There is a long discussion of the work of the Unite States Armed Forces Epidemiological Board (1941) an the value of its contributions in the field of preventiv medicine. The Board set up a number of commission for the study of special problems of importance for th armed forces and it is suggested that such researc commissions might be established to carry out th future tasks of preventive medicine in other fields.

Some of these tasks are described at some length with an account of the detailed study in preventiv medicine being carried out by the School of Health University of Michigan, of the health and disease o the community of 8,500 persons in Tecumseh, Michigan

M. E. Delafield

LANCET. 1960, Apr. 9, 819–22. **Israel and her Health Services 1948–1958.**

EPIDEMIOLOGY

BOYD, J. T. **Meteorological Conditions and Mortality.** [Abridged.] *Proc. Roy. Soc. Med.* 1960, Feb., v. 53, No. 2, 107–8 (Sect. Epidem. & Preventive Med. 1–2), 1 fig.

The author of this abridged note took weekly indices of mortality, temperature, absolute humidity, sulphur dioxide pollution and smoke pollution for the London area, and comparable indices for mortality, tempera ture, humidity and fog for the East Anglia area, fo the winter months of each year from 1947 to 1954 and correlated them.

For London the indices most closely associated with mortality at age 45 and over, especially for respiratory and heart disease, were those of temperature and absolute humidity; correlation with sulphur dioxide

and smoke was much lower. For rural East Anglia the same findings were observed, and it therefore seems that "the urban atmospheric pollution, absent in East Anglia, has little effect on the general association between temperature, or humidity, and mortality".

In East Anglia fog had no bearing on mortality, but in London there was a marked association between fog and mortality at low temperatures. "It appears that the more serious effect of metropolitan fog, as measured by excessive increases in mortality, occur only when fog is accompanied by very low temperature conditions . . ." *Charles Wilcocks*

FERGUSON, T. **Mortality in Shetland a Hundred Years Ago.** *Scottish Med. J.* Glasgow. 1960, Mar., v. 5, No. 3, 107–12.

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

CALIFORNIA, STATE OF. Dept. of Pub. Health [MERRILL, M. H., Director]. **California's Older People—their Health Problems.** 50 pp., illustrated. [Numerous refs.] 1959. Berkeley 4: 2151 Berkeley Way.

The distribution of persons aged 65 years and over was very uneven in the counties of California ranging from 14% of the total population in 2 counties to less than 5% in four counties; in 17 of the rural districts over 10% of the population were aged 65 and over. With increasing age the social and economic conditions of the people change. Over one-half of the women aged over 65 and two-thirds of them aged over 75 were widows. The fall in income with increasing age was faster for females than for males. Since about 30% of the women aged 70 and over live alone a number of welfare problems are created—nutrition, medical care and other health problems. In a State-wide survey about 70% of the persons aged 65 and over reported some illness in the preceding 4 weeks, mainly of a chronic nature. 5% of the Californian population aged 65 and over are residents in institutions of various kinds, over half of them requiring medical and nursing care. Mental illness accounts for one-sixth of the institutional population. In general hospitals persons aged 65 and over receive about 2 days care per person per year with an average stay of 17 days. The age-group above 65 form 8% of the total population but they comprise 29% of the mental hospital patients. In nursing homes the chief causes of admission are paralysis following a stroke, heart and circulatory conditions, senility, fractures, rheumatism and arthritis and they form about three-quarters of the admissions. An increase in the number of beds for future needs is estimated at 16,400 for long term sickness and 25,000 for psychiatric illness. The onset of blindness in almost one-third of the persons receiving public assistance was between 45 and 65 and in one-half at ages 65 and over.

Chronic diseases have become more important as a cause of death among old people. The chief cause of death for ages 65 and over, for both sexes, was heart disease, the second and third most important cause of death at ages 65–74 was malignant neoplasms and vascular lesions of the central nervous system and at ages 75–84 this order was reversed. The accident death rate for both sexes at ages 65 and over was over 500 per 100,000 population.

The report concludes with a survey of the current efforts to meet the health problems of the old people. *W. J. Martin*

CHRONIC CARDIO-RESPIRATORY DISEASES

JÄRVINEN, K. A. J. & THOMANDER, K. **Long History of Heavy Smoking as a Factor causing Obstructive Pulmonary Emphysema.** *Ann. Med. Intern. Fenniae.* Helsinki. 1959, v. 48, No. 4, 211–17. [14 refs.]

In 10,760 routine mass radiography results in the Department of Pulmonary Diseases University of Helsinki there were 159 adult men and women in whom the X-ray findings indicated possible obstructive pulmonary emphysema. At a specially conducted clinical examination of this group 42 were in fact found to have obstructive pulmonary emphysema and 50 to have perfectly healthy lungs. These two groups had a similar age and sex distribution and are compared. Of the 42 in the affected group 36 (86%) were heavy smokers (15 gm. or more of tobacco per day for a minimum of 10 years) while of the 50 healthy persons 19 (38%) were heavy smokers. Division by sex showed 8 out of 11 affected women to be smokers, 6 of them heavy smokers (as defined) and only 2 out of 17 unaffected women were smokers (1 a heavy smoker). Chronic bronchitis was a feature of nearly all of the affected group and did not appear in the unaffected. It is concluded that bronchiolar irritation from chronic cigarette smoking causes obstruction of the lumen and results in the development of obstructive pulmonary emphysema. *A. Bradford Hill*

CANCER

TODD, G. F. & MASON, J. I. **Concordance of Smoking Habits in Monozygotic and Dizygotic Twins.** *Heredity.* 1959, Nov., v. 13, Pt. 4, 417–44.

3 groups of twins, from Tübingen, Berlin and Frankfurt-am-Main, whose names were on the register of the Münster Institute of Human Genetics, and classified as monozygotic or dizygotic, were asked their smoking habits, either by mail or personal interview. Those from whom answers were obtained [and in the largest group it was less than one-quarter] were grouped according to the similarity or dissimilarity of their present or past smoking. The basic data and the classifications made are set out in detail so that any worker can make his own calculations. The authors themselves set out several alternatives. Thus, taking as alike both of pairs who had *never* smoked or both of pairs who had *ever* smoked, whether occasionally or regularly, then 47 of 52 monozygotic pairs were alike (90%) compared with 25 of 32 dizygotic pairs (78%). A further analysis deals with the type of product smoked [though pairs of non-smokers are again included] and here, according to one form of analysis, about 70% of the monozygotic pairs are alike compared with about 50% of the dizygotic (and the difference appears to be of the order of 25–30% whatever form of classification is used). A number of factors which might have affected the comparability or representativeness of the two sets of twins are discussed and it is concluded that there is no reason to doubt that smoking habits are more frequently concordant in monozygotic than in dizygotic twins.

A. Bradford Hill

PLOC, S. & DVORÁKOVÁ, A. Perzistence 3,4 benzpyrenu v myších plicích. [**Persistence of 3,4 Benzpyrene in the Lungs of Mice**] *Československ. Hyg.* Prague 1960, v. 5, Nos. 2/3, 134–40, 4 figs. & 3 graphs. [18 refs.]

The English summary appended to the paper is as follows:—

"Hitherto the cancerogenic action of substances was usually tested by rubbing the tested substance into the skin or by injecting it under the skin of experimental animals. Because this method is not suitable for examining the cancerogenic properties of substances in the atmosphere, the authors elaborated a method of administering these substances into the lungs of mice.

"They investigated experimentally the persistence of 3,4-benzpyrene in the pulmonary lobes of mice. The results of the experiments indicate that inhaled 3,4-benzpyrene is removed from the lungs within a few days.

"Finally the authors discuss the problem how long 3,4-benzpyrene inhaled by man remains unchanged in the lungs or bronchial nodes."

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

GENERAL

AGUADE, R. & HILBURG, C. J. Experiencias en saneamiento rural en el Paraguay. [**Rural Sanitation Experience in Paraguay**] *Bol. Oficina Sanitaria Panamericana.* 1960, Feb., v. 48, No. 2, 98–113, 10 figs.

The English summary appended to the paper is as follows:—

"Adverse environmental conditions affect the economic, social and health development of the population. Economically, they keep an important portion of the population from reaching the productive stage of their life and thus deprive them of the opportunity to begin repaying the investment they represent. Socially, such conditions give rise to pessimistic or passive attitudes toward what might otherwise have led them to improve their living standard. And from the viewpoint of health, conditions of this nature are known to be the basic cause of the diseases that most endanger the human potential of a country: the diarrheal and hookworm diseases, to cite but a few.

"A review of the situation regarding water supplies shows that the first water supply system in the country is now under construction; almost all of the existing supplies are individual, and 50 per cent. have facilities within the house, the majority of them on the basis of bored wells. As regards excreta disposal, the beneficial effects of the two campaigns against hookworm disease undertaken in 1924 and 1952 are clearly evident, since 88 per cent of the homes have some kind of disposal system, chiefly latrines. However, such systems are in need of improvement.

"This situation has endured until now owing to the inadequate resources assigned for sanitation, on the part of both the state and the community, and to the imbalance in the activities of the health services, which emphasize medical care and maternal and child health at the expense of sanitation.

"The Ministry of Public Health of Paraguay, with these facts in mind, established certain priorities among the multiple activities of environmental sanitation, focussing attention first on the factors which cause most harm and for whose control effective technical and administrative procedures are available. This approach led to a concentration of efforts on the provision of abundant and readily-available supplies of drinking water and the proper disposal of excreta and waste.

"In 1956, for purposes of demonstration, the Ministry of Public Health, with the technical co-operation of PASB/WHO and the material aid of UNICEF, undertook a program of rural sanitation. For this purpose it offered advice and aid to the communities in improving the systems of water supply and excreta and waste disposal in the rural areas. Consideration was also given to the protection of existing wells and springs; the boring of deep wells; the construction of driven or drilled wells, equipped with hand pumps; and the construction of latrines and household systems for burying waste. The program was conducted on the basis of full and active participation of the community.

"The experience acquired in the program has enabled the Ministry of Public Health of Paraguay to prepare a Plan of Basic Rural Sanitation, which will serve as a guide in implementing sanitation activities in all local health services. This Plan also will have the collaboration of PASB/WHO and UNICEF."

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

KUNERTH, K. Erfahrungen mit einem vereinfachten Endo-Agar bei der Bestimmung von *E. coli*. [**A Simplified Endo-Agar in the Detection of** *Escherichia coli*] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Feb., v. 6, No. 2, 103–6.

The author carried out a series of parallel tests, with the bouillon-Endo used in the Bezirkshygieneinstitut at Halle and the so-called "water-Endo" in use in the Zentralinstitut für Hygiene in Prague. Plates of each type of medium were inoculated with pure cultures of 2 types of *Escherichia coli* and one salmonella strain. No difference was detected in the salmonella colonies but the *E. coli* colonies on the water-Endo showed a marked metallic lustre not visible in those on the bouillon-Endo. The IMVC reactions of both types of colonies were the same. Further tests were done with water samples which had been deliberately contaminated with the 3 pure cultures and then allowed to stand for 48 hours at room temperature. Again the colonies on the water-Endo showed the characteristic metallic lustre not present on the bouillon-Endo. Plates of each type of medium were inoculated from 268 enrichment medium cultures which showed clouding and gas formation, obtained in the course of examining water samples. In the main there was good agreement in the results on the 2 media but the *E. coli* colonies on the water-Endo showed the characteristic metallic lustre 5 times as often as those on the bouillon-Endo. Growth of irregular and intermediate forms was more frequent on the bouillon-Endo. Growth on the water-Endo of *E. coli* was found to be very clear and the characteristic appearance of the colonies easy to recognize. Detailed instructions are given for the preparation of the water-Endo medium, the composition of which does not appear to differ materially from Endo-Agar Formula II which is available in dehydrated form given in *Standard Methods for the Examination of Water and Sewage and Industrial Wastes*, 10th Edition, p. 369, 1955 [this *Bulletin*, 1955, v. 30, 732]. *E. Windle Taylor*

GYLLENBERG, H., NIEMELÄ, S. & SORMUNEN, T. **Survival of Bifid Bacteria in Water as compared with that of Coliform Bacteria and Enterococci.** *Applied Microbiol.* Baltimore. 1960, Jan., v. 8, No. 1, 20–22.

It has been suggested that *Lactobacillus bifidus* may be a suitable indicator of faecal contamination of food and water. Human excreta abound with these organisms [this *Bulletin*, 1957, v. 32, 475] and so far as is known they do not grow in other natural environments. In this study their survival is compared with coliform organisms and enterococci by suspending faeces in water and estimating the survival rates. The results obtained indicated that the bifid bacteria behaved similarly to coliforms in water except that the former did not multiply whereas the latter showed some initial increase in numbers.

It is to be noted, however, that bifid bacteria occur in the faeces of man in much higher numbers (10 to 100 times) than coliform organisms and enterococci. This ratio decreases rapidly in warm conditions (18–20°C.) in polluted waters but more slowly in cold waters 4–6°C.).

Clearly more work is required on this subject of the significance of the occurrence of bifid bacteria in water.

E. Windle Taylor

MEDREK, T. F. & LITSKY, W. **Comparative Incidence of Coliform Bacteria and Enterococci in Undisturbed Soil.** *Applied Microbiol.* Baltimore. 1960, Jan., v. 8, No. 1, 60–63. [10 refs.]

This paper has a strong bearing on the investigation of pollution of water.

In recent years bacteriological media that are more efficient for the isolation of enterococci have been developed, for example dextrose azide broth as a presumptive medium and ethyl violet azide broth for confirmation. A study was made to determine to what

extent the coliform group and enterococci are present in undisturbed soils that had not been manured for 60 years. 369 soils were taken from areas adjacent to 4 Western Massachusetts reservoirs. Samples were taken at depths of 1–3 inches and examined for coliform organisms and enterococci. Almost three-quarters (73·4%) of the soil samples contained coliform organisms but in only 5 samples (1·4%) was the presence of *Escherichia coli* confirmed. Enterococci were found in 8 (2·2%) of the 369 soil samples examined.

The investigation has revealed that coliform organisms other than *E. coli* are frequently present in soil which is apparently undisturbed. The isolation of *E. coli* and enterococci was very infrequent and may have indicated the chance pollution of the soil by a bird or other wild animal or surface or sub-surface drainage. *E. Windle Taylor*

KELETI, J., VYMĚTAL, F., ABSOLONOVÁ, O. & POSPÍSIL, J. Problematika dojčeneckej methemoglobinémie v Československu. [**The Problem of Methaemoglobinaemia in Infants in Czechoslovakia**] *Československ. Hyg.* Prague. 1960, v. 5, Nos. 2/3, 152–9, 1 map.

The English summary appended to the paper is as follows:—

"The authors present detailed data on the incidence of methaemoglobinaemia in infants, recorded hitherto in 314 infants and caused by a high nitrate concentration of the drinking water in Czechoslovakia. Subsequently the authors discuss the water supply of some areas where the disease is most frequently encountered whereby it was revealed that in the Prague region from 16,008 water specimens investigated 69·9% had a concentration above 35 mg./l and on the Žitný ostrov 77·9% from a total of 131 samples investigated.

"An analysis of infant nutrition revealed that in rural districts the use of artificial feeding is increasing rapidly. From 149 infants examined on the Žitný ostrov only 31·6% were nursed by their mothers for longer than six months. In the present paper the authors evaluate also the effect of the high nitrate concentration of the drinking water on the methaemoglobi level in the children examined. From 17 children age 1–2 years 13 had a raised methaemoglobin blood leve without signs of cyanosis or abnormal signs in thei physical or mental development.

"Next the authors describe the clinical course an the results of the treatment of methaemoglobinaemi of infants in this country. Subsequently they analys in detail deaths in infants caused by methaemoglo binaemia and also mention the results of retrospectiv investigations of infants' deaths from this disease.

"Finally they evaluate the results of hitherto use measures to prevent methaemoglobinaemia in infant and recommend that for the preparation of infants foods suitable sources of drinking water should b sought in rural areas with the assistance of hygiene an epidemiological stations."

KNOTEK, Z. Ke vzniku alimentární methemoglobinémi po použití vody obsahující dusičnany. [**On th Development of Alimentary Methaemoglobi naemia after the Consumption of Water contain ing Nitrates**] *Československ. Hyg.* Prague. 1960, v. 5 Nos. 2/3, 160–65, 5 graphs. [13 refs.]

The English summary appended to the paper is a follows:—

"In the present communication the authors ar drawing attention to the necessity to study the patho genesis of alimentary methaemoglobinaemia and it prevention. They have demonstrated the effect of pH on the reducing capacity of faeces, the different bac terial capacity of the faecal flora to reduce nitrates i adults and infants and the increased ability to reduc nitrates in some infants. As a result of preliminar data the author assumes that this difference is due t the fact that the reduction is continuous. It is up t future research to confirm this theory and to revea what causes this continuous reduction. When invest gating the effect of $MgSO_4$, corresponding to the degre of different permanent hardness, the author foun higher reduction values in vitro. From this he con cludes that $MgSO_4$ acts a growth factor."

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

PUBLIC HEALTH LAB. SERVICE. **Committee on Bathing Beach Contamination** [MOORE, B., Chairman]. **Sewage Contamination of Coastal Bathing Waters in England and Wales. A Bacteriological and Epidemiological Study.** *J. Hygiene.* 1959, Dec., v. 57, No. 4, 435–72, 4 figs. [60 refs.]

This paper summarizes the bacteriological studies made during the previous 5 years by members of the committee working on material from more than 40 popular bathing beaches round the coast of England and Wales, the waters of the great majority of which were subject to contamination with sewage. Surveys for the rough grading of beaches were generally planned to ensure representative sampling from th areas on the beaches where bathing actually too place and, whether the assessment was made on th results of the presumptive coliform test or on faeca *coli* counts, a similar ranking order was obtained. Th median presumptive coliform counts of the differen coded beaches varied from 40 to 25,000. Meteoro logical and other factors played a part in the degre of pollution of bathing waters. The effect of a onshore wind on an exposed coast in driving sewag on to the beaches is well known and also the effec of heavy rainfalls causing part of the sewage to by pass the comminutor and be discharged directly throug storm water overflows to contaminate the beaches.

The isolation of pathogenic organisms from sea water was restricted to members of the salmonella group in the main, although *Staphylococcus aureus* was occasionally isolated. A high proportion of the samples examined yielded small numbers of salmonellae; as many as 40% of the samples containing over 10,000 coliforms per 100 ml. sea-water were found to contain salmonellae. The preponderance of isolations of *Salmonella paratyphi B* greatly exaggerates the importance of this organism in the present context; the same laboratory might continue to isolate it in a long series of examinations of samples from the same source. The same might also apply to some of the other salmonella serotypes isolated; there were 33 different species and this may be taken as evidence of the wide distribution of these organisms.

A small series of samples was examined for the presence of poliovirus with negative results, but special concentration methods to counteract the large dilution factor were not employed so that failure to isolate the virus was not unexpected. A statistically controlled epidemiological study of the bathing histories of 150 poliomyelitis cases in children living permanently by the seaside gave no evidence, however, that sea bathing played any part in causing the disease.

There were, however, 4 cases of paratyphoid fever which could have been due to bathing in sea-water infected with paratyphoid B; epidemiological and phage-typing data fully support this probability.

The general conclusions of the committee were that bathing in sewage-polluted sea-water carries only a negligible risk to health and where the risk is present it is probably associated with chance contact with intact aggregates of infected faecal material. The isolation of salmonellae from sewage-contaminated sea-water is more important as a reflexion of the distribution of the various serotypes in the populations from which the sewage is derived than as evidence of added risk of infection in bathers. Unless the water is so fouled as to render the bathing beach aesthetically revolting it would seem that public health requirements are reasonably well met by the present general policy of improving grossly insanitary beaches and preventing as far as possible the pollution of the waters, at any rate during the bathing season, with undisintegrated faecal matter.

[This important paper contains the results of a planned investigation by a large team of experienced bacteriologists working over a long period. A very considerable amount of carefully acquired and valuable information was collected from this large scale investigation, one of the most comprehensive undertaken in this field. The conclusions of the committee after very full consideration of all the evidence available and in the light of present day knowledge must be accepted as reassuring in spite of the unaesthetic factors involved. A recent report of a similar investigation, but on a much smaller scale, of popular bathing beaches in Poland [BUCZOWSKA, this *Bulletin*, 1960, v. 35, 426] gave results which were not dissimilar and the conclusions about the dangers to health were of the same order. The Polish report was also concerned with the frequency of salmonella isolations from the waters of bathing beaches, but it indicated that the distribution of the serotypes in the bathing waters was in accordance with the sickness and carrier records of the areas involved. Although one would not dispute the correctness of MCCULLOUGH and EISELE's figures [*this Bulletin*, 1951, v. 26, 1118 *bis*; 1952, v. 27, 785 *bis*] under the terms of their experiments and with the strains of salmonellae they used for the estimation of infecting doses for man, our information on this subject is very inexact. While epidemiological evidence may suggest that institutional cross-infection with salmonella organisms depends on a much smaller infecting dose than any indicated by McCullough and Eisele, there are no exact figures to support this. It seems important to bear this point in mind. Nevertheless on the evidence produced by the committee, it must be agreed that the minimal risk incurred by bathing in sewage-contaminated sea-water is one of exceptional chance.]

H. J. Bensted

MEDICAL RESEARCH COUNCIL. **Sewage Contamination of Bathing Beaches in England and Wales.** *Med. Res. Council Memorandum No. 37.* pp. iv + 24. 1959. London: H.M. Stationery Office. [2s. 6d.]

This memorandum is concerned with the same problems that are dealt with in the report of the Committee of the Public Health Laboratory Service on Bathing Beach Contamination (see above), but because the subject has aroused more public interest than most problems of hygiene, and is of special interest to local authorities, it was decided to present a memorandum designed particularly for the non-specialist reader. The detailed technical findings and the epidemiological considerations are more fully dealt with in the other publication.

Of necessity the memorandum contains a considerable amount of general background, not present in the technical communication, in order that the problems under discussion may be more readily appreciated by the non-specialist reader so that he can understand such technical points that have to be introduced. Some of the obvious fallacies of ascribing various diseases to sea bathing are indicated and recommendations are made where, under certain conditions, gross visible faecal contamination of the beaches may occur. It is explained, however, that full treatment of sewage does not result in a sterile, or pathogen-free, effluent and the findings of the investigation do not provide grounds for any attempt to render bathing waters free from faecal bacteria.

The main conclusion of the committee after full consideration of all the bacteriological and epidemiological evidence is the reassuring statement that bathing in sewage-polluted sea water carries only a negligible risk to health or in the words of the memorandum: "the risk . . . can, for all practical purposes, be ignored."

H. J. Bensted

MOORE, B. **Some Bacteriological Aspects of Sewage Pollution of Bathing Beaches.** *Roy. Soc. Promotion Health J.* 1959, Nov.–Dec., v. 79, No. 6, 730–34. Discussion 734–5.

This paper is in fact an address at an Isle of Wight meeting of the Royal Society of Health in which the

author discusses the dangers of accepting bacteriological findings arising out of the general use of the coliform test in water examinations without a very full understanding of all the problems involved. In other words the level of contamination by faecal *coli* of a particular sample of sea-water cannot be judged in terms of drinking water standards, but considered in relation with a number of other factors it can be a useful guide in certain sanitary engineering projects.

In considering the risks of bathing in sea-water which is contaminated by sewage it is not so much the fact that a certain pathogenic organism is present in the sewage that is of prime importance but whether its presence there constitutes a potential danger to health as a practical proposition rather than a theoretical possibility. A bathing beach may be condemned on aesthetic grounds with justification, but condemnation on bacteriological findings without the fullest support from an intensive study by experienced epidemiologist is to be deprecated. *H. J. Bensted*

KABLER, P. **Removal of Pathogenic Microorganisms by Sewage Treatment Processes.** *Sewage & Indust. Wastes.* Wash. 1959, Dec., v. 31, No. 12 1373–82. [43 refs.]

This article presents a comprehensive review of research into the removal of pathogenic micro-organisms in sewage treatment. Figures are given for the percentage removal of different kinds of micro-organisms by the different processes and it is concluded that the effluents from all processes contain a proportion of each kind of incoming pathogen. The remainder of the article deals with methods of removing these remaining organisms by chlorination and sedimentation. There is a very useful summary of the present methods of enumerating pathogenic bacteria, viruses and fungi.

A. James

ATMOSPHERIC POLLUTION

STEPHAN, D. G., WALSH, G. W. & HERRICK, R. A. **Concepts in Fabric Air Filtration.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 1–14, 12 figs.

Fabric filters can give highly efficient control of air pollution at low cost, but little information is available about air filtration as it occurs within commercial equipment. The authors discuss the concepts of filter resistance and permeability. They have measured local air speeds and local dust masses within filters, and their consideration of the results obtained raises various points concerning the design and cleaning of filters.

The paper is highly technical and should be read in full by those concerned with the design of filters.

Thomas Bedford

PORT, SHIP AND AVIATION HYGIENE

BARCLAY, A. Y. **The Men who Sail the Ships.** *Trans. Ass. Indust. Med. Officers.* 1960, Jan., v. 9, No. 4, 129–33, 1 fig.

This paper gives a comprehensive description of the way that the medical care and supervision of the men of the Merchant Navy is carried out, particularly by the medical officers of the Shipping Federation.

The Shipping Federation provide crews for the majority of British ships and the function of the medical department is to ascertain that the men are fit before they sail. Two tables show the size of the industry and the number and types of service performed by the Medical Officers at Glasgow 1958–59. New entrants and re-entrants to the industry are given a full medical examination with X-ray screening. A pre-shipment examination is equivalent to an Army FFI (freedom from infection) examination.

Seamen who become sick ashore are brought in periodically to note the progress of treatment. National health facilities are extended to non-resident members of ships crews both British and foreign: a table is given showing the number of such services performed during 1958.

In addition to new entrants and re-entrants all regular seafarers who are on a company service contract or an establishment contract are examined by X-ray on renewal of these contracts every second year.

Anti-cholera inoculations, TAB and smallpox vaccinations are carried out both in ships and in the department. Table IV gives the number done in each.

Standards of medical fitness are laid down by the National Maritime Board and are practically identical with those of the National Service examination; the Shipping Federation medical officer should have a detailed knowledge of the various jobs in a ship and what each entails.

The psychological stresses peculiar to seafarers are enumerated; the necessity for the medical officer to have some knowledge of shipping routes in order to assess climate stress is also pointed out.

Complaints about food are now comparatively rare, on the other hand complaints about the drinking water are far more common. The difficulty of decidin

whether or not men suffering from peptic ulcers should be allowed to go to sea or not is discussed and also those who have had a gastro-enterostomy or partial gastrectomy done.

Working hours vary immensely particularly in tugs and the tradition of the sea sometimes requires the crews to work long hours when distress signals from other vessels are received.

Attention is drawn to the difficulty of collecting reliable figures in relation to the health hazards of seafarers and several examples are given; it is pointed out that it is unsound to compare statistics of seafarers with other industries, owing to the fact that shipping is so diversified.

The evidence of pulmonary tuberculosis in the port of Glasgow among new entrants is 6 times higher than in any other port in the United Kingdom. Only 3 cases of bronchogenic carcinoma of the lung have been discovered, although it can be assumed that seafarers smoke more heavily, as they are in receipt of duty-free cigarettes.

Tables are given showing the evidence of pulmonary tuberculosis by age-groups, and one table refers to the results of X-ray examination of a comparatively small number of Asians: this indicates that pulmonary tuberculosis is extremely common among these people.

This paper shows how routine and frequent examination of seamen is carried out by the Shipping Federation, and how prophylactic inoculations are in constant use. Diet is good and accommodation improving; tuberculosis appears to be on the wane, and the cause of much of the illness would appear to be the improper use of leisure. *E. R. Peirce*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

MINISTRY OF LABOUR. **Report on Safety and Health in the Building and Civil Engineering Industries 1954–1958.** Cmnd. 953. 30 pp., 6 figs. 1960. London: H.M. Stationery Office. [1s. 6d.]

The annual reports of the work of the Factory Inspectorate include sections on accidents at building operations and on works of engineering construction, but it had been felt that a report giving more detailed information should be made from time to time. This, the first of such reports, covers the years 1954–1958, and future reports will cover periods of 3 or 4 years.

There has been difficulty in preparing the report owing to the inadequacy of some of the accident statistics available to the Ministry. A revised form of accident report was brought into use in January, 1959, and the statistics in future reports should be more useful.

Over the years covered by the report the numbers of accidents increased, but on account of the nature of the statistics it is difficult to appraise the significance of the rise. The numbers of accidents cannot be expressed in terms of the numbers of operatives employed or at risk, or of the volume or type of work in progress. It is impossible to gauge the effect of improved compliance with legal requirements about the reporting of accidents. One thing is clear, however. There are still far too many accidents on construction work, and if these industries are to be made safer both employers and operatives must use every endeavour to that end.

The first chapter of the report sets out the most important points of the law concerning safety and health in these industries, and in the second chapter the accident statistics are set out. Further short chapters deal with training in safety, with health and with welfare. *Thomas Bedford*

JEFFERYS, Margot & WOOD, C. H. **A Survey of Small Factories.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 10–24, 12 figs.

Of some 234,000 factories registered in Great Britain, only 5% employ more than 100 workers, and no less than 83% employ 25 persons or fewer. An important organizational problem of the occupational health services centres in the provision which is practicable for small factories and workshops. The present enquiry was designed to answer 3 questions: What are conditions like in these small firms? What medical services, if any, do they possess or make use of? Is it worth while to run an industrial health service on a collective basis?

Part of the ward of a metropolitan borough, comprising mixed residential housing and small-scale industry, largely developed round the beginning of the century, was selected for study. There were 50 registered factories. A questionnaire was designed to provide information relating to the number and type of employees, the fabric and age of the premises, hazards involved in the work, medical and first-aid arrangements, and the routine inspection of various authorities. 48 factories responded and 45 allowed visits. The field investigators, visiting in groups of 3,

were members of a study group of doctors and nurses in the Department of Public Health of the London School of Hygiene and Tropical Medicine, and the exercise was part of the teaching programme for the Diploma in Public Health.

Construction of the factories was varied and the processes diverse. Only 18 out of 48 were originally designed for their purpose. 20 were concerned with light engineering; and the remainder covered a wide range of industry, including textiles, food manufacture, toys and precision instruments. Survey assessments were for the most part subjective, but the results provide an interesting, if incomplete, picture of the conditions of work. Sanitary and washing arrangements were thought inadequate in at least 8 factories; 3 were unduly noisy; and 2 decidedly cold. 10 were dirty by any standards, including a shoe-maker's shop "where fragments of the employees' lunch collected among the days' old accumulation of odd pieces of leather". Artificial lighting was usually sufficient in the working area, but not on stairs and in passages. There were a number of hazards. In regard to dust and fumes, exhaust ventilation, where provided, was sometimes not efficient. Chemicals used involved well recognized toxic hazards such as carbon tetrachloride, naphthalene and kerosene, but the employees' attitude towards them seems to have been often casual in the extreme. Power-driven machinery, however, was usually well safeguarded. First-aid boxes were produced in 43 factories, but in 12 the contents were considered inadequate. Accidents in the previous year corresponded to a rate of 17 per 1,000, somewhat below the national figure. But in 21 factories, mainly the very small ones, there was no accident book, and hence no record and presumably no official returns. This leads the authors to question the validity of low accident rates in small factories, as shown in the Report of the Chief Inspector for 1954. There was little non-statutory health provision. No nurse was employed. 3 factories had working arrangements with general practitioners, but in only one case did this extend to an interest in the general environment.

In their conclusions, the authors thought it unrealistic to propose a full-scale co-operative occupational health service. In the particular area surveyed, which gave ready access to the casualty departments of two neighbouring hospitals, there was on the therapeutic side little justification for this. As a short-term policy they would propose, without specifying in detail the necessary administrative arrangements, a system of closer inspection by a single individual, akin to public health inspection in relation to dwelling houses. Small factories often have more in common with family enterprises than large-scale industry; and the owner is usually also in charge of records, while at the same time being foreman and co-worker, and has little appreciation of legal requirements, or of the separate functions of the various inspectors at present responsible for aspects of industrial health and hygiene. In this way, improved first-aid arrangements in material and personnel, and compliance with Health and Safety Regulations, could be enforced more adequately. In the long term they see the provision of flatted factories by local authorities as the answer to many of the environmental problems.

[See also the Halifax survey, this *Bulletin*, 1958, v 33, 754.] *F. Grundy*

MORRIS, J. N. **Occupation and Coronary Heart Disease.** *Arch. Intern. Med.* 1959, Dec., v. 104 No. 6, 903–7.

Some of the epidemiological studies of coronary heart disease undertaken by the Social Medicine Research Unit of the Medical Research Council were the subject of this paper read at a symposium on coronary disease organized by the American Medical Association in June 1959.

Data collected for 10 years 1949–59 relating to London bus drivers and conductors show that at ages 35–49 years the average annual death rate, due to sudden death as the first clinical manifestation of disease, was 0·56 per 1,000 among drivers compared with only 0·17 per 1,000 for conductors. In older age-groups the relative difference is not so great; the rates at ages 50–64 years were 1·9 and 1·2 per 1,000 respectively. Similar occupational differences have been reported for post office workers. Men in sedentary jobs (clerks, minor officials and telephone operators) had more rapidly fatal cardiac infarction than physically active postmen when the comparison was confined to men under age 50 years.

A table based on the 1949–53 occupational mortality data collected by the Registrar General for England and Wales shows for each of the conventional social classes the death rates in "light", "active" and "heavy" occupational sub-groups. In both age-groups 45–54 and 55–64 years, the coronary heart disease (No. 420, *International Statistical Classification of Diseases, Injuries and Causes of Death. W. H. O.* [see this *Bulletin*, 1949, v. 24, 720]) death rates for each social class were highest in the "light" and lowest in the "heavy" occupations. Similar and further conclusions were drawn from a national survey of post-mortems in Great Britain in 1954–56 which showed that coronary heart disease was most frequent in "light" workers aged 45–70 years. Moreover, among 3,800 post-mortems on persons whose deaths were from causes other than coronary heart disease, ischaemic fibrosis of the myocardium was more often discovered among "light" workers than others in the age group 45–59 years. Prevalence rates for large healed infarcts (usually 1· cm. in diameter and transmural) were 2·3% in "light" 1·3% in "active" and 0·5% in "heavy" occupations while for all types of ischaemic fibrosis the rates were 10·0, 5·5 and 3·9% respectively.

High blood pressure was more common among bus drivers than conductors; at ages 40–49, 50–59 and 60–6 years the proportion of drivers with systolic pressure over 180 mm. Hg were 8·8, 12·5 and 16·4% compared with 2·1, 6·8 and 14·8% respectively for conductors. In the same age-groups diastolic pressures of over 10 mm. Hg were recorded for 3·5, 12·5 and 12·3% of drivers compared with 0, 4·3 and 11·1% respectively of conductors. The necropsy survey afforded evidence that hypertensive "light" workers were particularly

liable to coronary heart disease. In the 3,800 reports of deaths due to causes other than coronary heart disease there were 1,800 in the age-group 45–59. When essential hypertension was reported in this group of 1,800, it was accompanied by report of ischaemic myocardial fibrosis in 24% of the post-mortems on "light" workers, 9·4% of those on "active" workers and 2·2% of those on "heavy" workers. When in the same 1,800 post-mortems no mention of hypertension was made the prevalence of ischaemic myocardial fibrosis was 6·6% for "light", 3·8% for "active" and 3·7% for "heavy" workers.

Some preliminary observations are made on work at present being undertaken on diets of London busmen and on the effects of obesity, constitution and self selection for occupation. Professor Morris suggests that all these studies lead to the conclusion that "physical activity/inactivity is a general factor of cardiovascular health in middle-age, being related to the frequency of coronary heart disease and coronary occlusion, to blood pressure and blood lipid levels, to obesity, and possibly also to diabetes. Coronary heart disease may therefore be in some measure a deficiency disease." *E. A. Cheeseman*

ARCH. MALAD. PROFESSIONNELLES. Paris. 1959, Sept.–Oct., v. 20, No. 5, 673–99. 5es Journeés Nationales de Médecine du Travail. Lyon, 9–10–11 octobre 1958. 3e rapport. Adaptation au travail des jeunes handicapés. **[Fitting the Handicapped Juvenile for a job]**

The Industrial Medical Officer and the Young Handicapped Worker (M. L. CHRISTIAENS, pp. 673–683).

Christiaens introduced the subject by estimating the number of young people in this category in France at the high figure of 10%. He pointed out that in a large family the handicapped child is frequently given extra attention and he made a plea that industrial medical officers should show the same interest when such a juvenile presents himself for a job. With advances in paediatric medicine the number of handicapped juveniles fit to do a job of work was likely to increase.

He went on to say that many of those specialists concerned with the treatment and rehabilitation of these youngsters seem to ignore the existence of industrial medicine and so of the help and co-operation which could be obtained in fitting their patients to suitable employment. He deplores the lack of liaison between the school and other medical services and those doctors engaged in occupational medicine.

During childhood the handicapped are often too protected and they would derive much benefit from a determined effort to encourage them to their full capabilities. He described a youth with a spastic paraplegia but with a high I.Q. on whom large sums had been spent to provide him with pastimes, money which could have been devoted to training him in accountancy —a career which he was quite capable of following.

The danger of segregating these handicapped individuals is stressed, their protected lives leaving no scope for the initiative which many are fully capable of developing. He mentions a home for handicapped children to which teachers had to be brought from outside, whereas most of the children could quite well have attended the local school with consequent benefit and a realization of the independence which they could achieve.

The author went on to consider the various classes of handicaps and pointed out the importance of finding out what an individual can do in terms of function, such as using a screwdriver, and not to worry too much about the anatomical details. He asks that industrial medical officers should make special studies of their factories and to note all jobs which can and should be done by handicapped people.

More and more opportunities can be made for the blind to earn their own living and we should no longer think in terms of piano tuning and similar traditional callings. Switchboard operation is limited by the number of businesses large enough to have them, but with new electric aids (tape recorders and dictaphones) shorthand and typing is now a possibility. Since 1925 50 blind people have worked in Ford's factory at Detroit and in England there are 160 blind shorthand typists, half of these being in Government employment.

Although the difficulties are not so great in placing the partially sighted, the provision of special lighting, avoidance of strain in those pre-disposed to retinal detachment, and avoidance of dusty atmospheres for those with keratitis, pose special problems.

In discussing the working conditions of deaf mutes, the deaf and the partially deaf, the author stresses that it is not a case of just helping for philanthropic reasons but in order to make the fullest use of their economic potential.

Epileptics are considered in 3 classes—the first with only occasional attacks posing no great problem. The second group with frequent attacks not responding to treatment do need special centres where they can work in safety or employment under special conditions such as market gardening. The third and most severe group can only work in special centres.

The last categories discussed consisted of the mentally handicapped, the social misfits and those with chronic illnesses, such as heart conditions, diabetes, nephritis and other conditions. Suitable jobs for the mentally retarded were woodwork, building, packing and some forms of simple metal work. In the case of unstable personalities he stressed that regular work, with the security and fellowship that it offers, could be their salvation. The importance of the role of industrial medical officers in supervising those workers with diabetes mellitus was stressed. The author makes a final plea for a policy of finding out what people can do rather than one of merely imposing restrictions.

The Role of the Industrial Medical Officer in the Supervision of Handicapped Juveniles in the Building Industry (A. SIVADON and R. DELMAS, pp. 684–690).

In this paper the authors discuss the employment of handicapped juveniles in the building industry. They

point out that it would be most useful to have a clear picture of the numbers already in such employment and to have an analysis of the trades in which they have made their way successfully. The authors state their intention of making such a survey.

Building operations are often carried out in the open, exposed to the elements, often in noisy conditions and in dusty atmospheres. The workman may have to adopt a variety of working positions, work at heights and climb ladders. It is also pointed out that much of the building material still has to be manhandled into position.

Another important consideration is that workers may have to travel considerable distances to the building sites.

All these considerations limit the extent to which those with physical handicaps such as heart disease, orthopaedic conditions and lung affections can be considered for such work. Those who have successfully overcome these difficulties are usually those who have worked in the trades before their pathological conditions have developed, and have been able to readapt themselves to a job with which they are familiar.

The authors conclude that there is very little place for the physically handicapped young person in the building trade.

Quite a different state of affairs exists in the case of psychiatric disorders; many of those affected are able to work in the building trade, while other types of work are barred to them. The unstable personality usually finds just those conditions of work which are most favourable, *i.e.* working in small groups, often in the open air and with frequent changes of scene.

In discussing the part that the industrial medical officer can play in the supervision of young people at work, the authors make the interesting suggestion that the fit adolescent is nevertheless to be regarded as handicapped when compared with his adult contemporaries. Those of not yet fully developed physique and strength not only do a full job but their leisure activities are often excessive in the way of sports, late nights, dances, etc. In addition the young worker is developing psychologically and has the problems of puberty to work out. At this age he is tempted to take risks both at work and in his leisure hours.

The very fact that at the age of 14 (in France) a youngster has to take decisions on the nature of his future career is itself sufficient (the authors consider) to cause serious emotional conflict.

The importance of close links between the industrial medical officer and management and the mutual respect engendered is stressed. Managements are nervous of employing handicapped people and unproved youngsters in particular. The industrial medical officer can explain the facts and obtain the co-operation of employers.

The organizations concerned with the welfare of these handicapped youngsters should establish close relations with the industrial medical officers in their district in order that their efforts shall have a really worthwhile result, and extra attention should be paid in the school years to ensure that educational backwardness is not added to a physical handicap.

A Preliminary Report on the Results of Eight Years' Work at a Rehabilitation Centre (Cahuzac, Bardier, Biardeau, Nichil, Ousset and Christol pp. 691–695).

This is a report of the results obtained at a rehabilitation centre (Ramonville Saint-Agne) for young people and the article consists almost entirely of a series of tables.

The report is limited to those who had reached the age of 16 years and had left the centre and shows their subsequent progress. The material was obtained from questionnaires. 133 were sent out and 75 were received. The questions were:—

1. What work are you doing?
2. Is it your first job?
3. Do you think that your pay is adequate?
4. Did you carry out further studies after leaving the centre?

Of the 75 who replied 32 were not working and were not pursuing further studies. 20 were working and of these, 18 felt that they were adequately remunerated. 5 worked in offices, 6 in farming and 7 were craftsmen. The remaining 23 were still studying. There were 3 unemployed at the time of receiving the questionnaire who had worked at some time since discharge from the centre as postmen. They were refused permanent employment because of their physical handicap, although they had been quite capable of carrying out their duties.

Detailed tables are given, the best results, as one would expect, are among the orthopaedic cases. Spastic and athetotic subjects were very difficult to place.

A plea is made for legislation to facilitate the integration into the working community of these handicapped individuals.

The Young Worker with Dermatitis (G. Chanial and J. Rivoire, pp. 695–696).

This is a report on a short investigation into the incidence of follicular dermatitis in an engineering workshop with particular exposure to mineral oils. The incidence in relationship to a past history of skin trouble of any sort is shown.

60% of all the workers (male and female) had oil acne. Those with a past history of skin trouble all had marked folliculitis (100%) but of those with a history completely clear of skin conditions, only 36% had oil acne. Conditions which were significant in the past history included acne vulgaris, seborrhea, eczema, pityriasis and sweating disorders.

On the basis of these findings the authors suggest that young people with a history of skin trouble should be advised and guided into occupations carrying no dermatitis hazards.

The Role of the Industrial Medical Officer in Advising on the Employment of Handicapped Juveniles (M. Michel, pp. 696–699).

The author discusses the problems posed in advising on the employment of handicapped people in the

French railway system. The small isolated units such as country railway stations present the biggest problems because of the scarcity of alternative jobs. In each region one of the doctors has special responsibility for handicapped workers and with the co-operation of the area management, each case is studied and a solution sought.

The author describes a system of punch cards already in use for several years. All the jobs in the railway system have been analysed and the physical and other requirements inserted on a card. When a doctor has to recommend the placing of a handicapped person, he can quickly pick out all the jobs which are suitable for the individual concerned. The suggestion is made that this system could be profitably employed in industry generally. *Francis Seager*

CHAVASSE, P., SAULNIER, G. & NICKLÈS, H. La lutte contre le bruit: protection des travailleurs contre les bruits et les vibrations. Principaux points à considérer dans les locaux à usages industriels et commerciaux. [**Control of Noise. Protection of Workers against Noise and Vibrations. Principal Points for Consideration in Industrial and Commercial Undertakings**] *Ann. Occup. Hyg.* London. 1959, Apr., v. 1, No. 2, 186–202, 11 figs. [26 refs.]

In this article the authors review the methods available to industry for the reduction of noise, and where this is impracticable for the protection of the workers from its harmful effects.

Examples of industrial deafness are given and the nuisance caused by noise in the neighbourhood of aerodromes and engine test plants mentioned, but no account of the actual physiology is given.

Quite rightly, emphasis is placed on the importance of good design and planning, but the authors recognize that this is a counsel of perfection and that efforts have to be made to reduce noise levels from existing machinery and installations.

The question is considered under the following headings:—

1. Alterations and improvements that can be made in the general surroundings—walls, ceilings, floors.
2. Choice of suitably designed machinery and alterations to existing equipment.
3. Proper maintenance of machinery and suitable methods of fixture.
4. Correct siting of machinery and of the operators.
5. Protection of the individuals.

The last can be achieved by proper application of all the measures previously discussed together with personal protection (ear defenders) where this is necessary.

The authors recognize the difficulties met with in practice in designing suitable appliances and ensuring their proper use. *Francis Seager*

COX, J., WOOLMER, R. & THOMAS, V. **Expired Air Resuscitation.** *Lancet.* 1960, Apr. 2, 727–30, 7 figs. [18 refs.]

A great deal of work has been carried out in the U.S.A. and other countries on the efficiency of expired air resuscitation but this is the first report of a controlled study to appear in Britain, undertaken on behalf of the Royal Navy.

22 experiments are reported in which the expired air resuscitation technique (by mouth-to-airway) was practised for periods ranging from 15 to 115 minutes on anaesthetized and paralysed subjects by "breath donors" who had never performed the method previously.

Continuous measurements were made of tidal volumes and of carbon dioxide concentrations in both the donor's and the subject's expired air during the course of each experiment.

Apart from the convincing experimental evidence, the various objections which have been raised to the adoption of the technique of direct insufflation have been considered and the conclusion reached was that the efficiency of expired air resuscitation for emergency use was such that it should be recommended as an alternative to the standard methods and, in some cases, it may be the method of choice. [It is noted that to overcome any aesthetic objections the mouth-to-airway technique was used instead of the direct mouth-to-mouth or mouth-to-nose techniques. The use of airways, particularly in lay hands, has been considered by COLLINS and SALAND (*New York State J. of Med.*, 1960, v. 60, 388) who report serious disadvantages in their use and cite 2 fatalities allegedly caused by the improper use of airways.] *L. M. Croton*

OCCUPATIONAL DISEASES

NAGELSCHMIDT, J. G. **Dusts and Lung Diseases.** Reprinted from *British Ceramic Res. Ass. Special Publication No. 23.* 1959, 27–38, 9 figs. Discussion 38–42.

This is the text of a lecture delivered, presumably, to representatives of the industry and an account of the discussion which followed. The subject is restricted to dust as a cause of lung disease and does not include diagnosis, disablement benefit or prevention. After giving information about the incidence of pneumoconiosis in Britain with special reference to the pottery and refractories industries, the author deals with such factors as the actions of different dusts, particle size, experimental silicosis and lung dust analysis. The 10 tables include some dealing with the rate and extent of production of fibrosis in experimental animals, and also with the amount of total dust and percentage of quartz found in human cases. While directed particularly at the pottery industry, this concise and well balanced account of the pneumoconiosis problem would be of interest to employers in other trades with a dust risk. *A. T. Doig*

GROSS, P. **An Immunologic Approach to the Pneumoconioses.** *Arch. Indust. Health.* Chicago. 1960, Mar., v. 21, No. 3, 228–32. [21 refs.]

A review.

ZWETKOW, L., HADJIOLOW, C., DALAKMANSKI, KOTSCHANKOWA, DOTSCHOWSKI, PANOW & MOTOLOVA, P. Untersuchungen über die Silikose, Silikotuberkulose und die anderen Berufskrankheiten unter den Arbeitern des Goldbergwerks "Slata" im Zusammenhang mit ihren hygienischen Lebens-und Arbeitsbedingungen. [**Silicosis, Silico-Tuberculous and other Industrial Disease in Mine Workers**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Feb., v. 6, No. 2, 74–9.

In this short paper by authors in Sofia, Bulgaria, there is a general account of the circumstances which may have an adverse effect on the health of workers in the "Slata" mine. There are short descriptions of atmospheric conditions in the mine, in the workmen's dwellings and in the open; the amounts of carbon monoxide and nitrous gases in the mine air after blasting operations; the amounts and particle sizes of the dust in the air; the ionization of the atmosphere and the diet and nutritional state of the workers of whom 39·2% of the healthy and 44·6% of those with silicosis were in negative nitrogen balance.

There is some account of the findings of medical examination of the mine workers [the number of these is not stated]. The incidence of silicosis which was 50·2% in 1951 was reduced by improvement in conditions of work to 29·7% in 1956. Pulmonary tuberculosis was found in 1·5% not only of the workers but also in the populations of the neighbouring villages. Among other conditions suffered by the workers were emphysema (3·92%), other respiratory affections (13%), arthritis and radiculitis (2·94%), injuries (16·5%) and suppurative skin diseases (3·3%).

These findings emphasize the need for much improvement in the conditions of work and circumstances of life of these mining workers. *M. E. Delafield*

SARTORELLI, E., GRIECO, A. & ZEDDA, S. Studio sulla mescolanza intrapolmonare dei gas nei silicotici e negli enfisematosi. [**Study of Intrapulmonary Mixing of Gases in Emphysematous and Silicotic Subjects**] *Med. d. Lavoro.* 1959, Dec., v. 50, No. 12, 766–80, 7 figs. [54 refs.] English summary.

The investigations reported in this paper were carried out on 76 men, of whom 15 were normal, 25 had emphysema and 36 silicosis. The normal subjects were classified into 2 age-groups and the emphysematous subjects were considered in 2 groups according to the stage of their lesions. The silicosis patients were divided into 4 groups—2p–3p, 2m–3m, 2n–3n and A(m-n)–B(m-n)—following the Geneva (1958) classification.

The authors describe the apparatus and technique which they employed. They plotted and analysed the curves of nitrogen clearance from the lungs when the subject was made to breath in pure oxygen through an open circuit. They determined the time taken by these gases to mix inside the lung and measured the volume of variously ventilated lung "compartments" which they expressed as a percentage of the residual functional capacity.

In some of the normal subjects, especially the younger groups, ventilation was so good as to allow a practically uniform mixture of the inspired and the alveolar gases. Where such uniformity was less complete, the alveolar volumes were found to represent one large compartment and some "accessory" smaller compartments.

Those who suffered from a chronic, obstructive, emphysema showed much less uniformity in the process of gas mixing within the lungs corresponding to a lowered ventilatory efficiency and this was more especially marked when the disease was most advanced. They found nothing to suggest a main, large, ventilatory compartment with smaller "accessory" sections of the alveolar system. The unequal ventilatory efficiency in different parts of the lungs of an emphysematous patient is most probably due to varying degrees of local bronchiolar obstruction and loss of elasticity in the alveolar walls.

In no case of silicosis could the authors demonstrate that there was uniform pulmonary ventilation as from one single compartment. In the subjects of types 2n–3n and A–B they found less uniformity of the alveolar ventilation; the gases took longer to mix and the curves suggested 3 separate alveolar compartments functioning at different rates and volumes. The intrapulmonary mixing of gases showed no significant departure from normal in 2p–3p and 2m–3m types of silicotic patients. In cases of advanced silicosis the lack of uniformity in the alveolar ventilation is, therefore, an important factor in causing functional insufficiency of the breathing process in such patients. Though the findings were somewhat similar in emphysematous subjects, the silicotic fibrosis unevenly impairs by itself the elasticity of the lung tissue and this affects the rate of intrapulmonary mixing of the gases.

J. Cauchi

KLOSTERKÖTTER, W. & BÜNEMANN, G. Quantitative Untersuchungen über die Lungenreinigung im Tierexperiment. I. Mitteilung. [**Quantitative Investigation of Lung Clearance of Dust in Animal Experiments**] *Arch. f. Hyg. u. Bqkt.* 1959, Feb., v. 143, No. 2, 112–24, 8 figs. [17 refs.]

A meeting of silicosis experts in 1955 (under the auspices of the High Authority of the European Coal Community) recommended further investigation of retention and elimination of dust by the lungs. After reviewing relevant previous work this paper describes experiments designed to obtain quantitative estimates of these functions.

Rats were exposed in an inhalation chamber to quartz flour No. 12 (SiO_2 content 98·9%) with a particle size-range of up to 30 microns and at a concentration of 50–90,000 particles per cc. of particles up to 5 microns. The animals were exposed for 6

hours daily and the mean lung SiO_2 content was estimated for groups of 5 animals killed after 1, 2, 5 and 8 daily exposures. Groups were killed at 24 hours, and then monthly from 1 to 5 months after the end of dust exposure. (Details of method of dust extraction from the lungs and chemical estimation of SiO_2 are given.)

The mean lung SiO_2 content after 1 day's exposure was 501 ± 80 μgm.; after 2 days' exposure 992 ± 100 μgm.; after 5 days' exposure 2,610 ± 270 μgm.; after 8 days' exposure 5,420 ± 16 μgm. as a mean of 14 rat lungs and 5,250 ± 450 μgm. as a mean of 5 rat lungs. This higher than expected value for the 8-day exposure group was thought to be due to lack of uniformity of dust concentration in the inhalation chamber. [These results are indeed extremely good for inhalation experiments.] In a group of 10 rats killed 5 months after the end of 2 days' exposure 37% of the dust had been eliminated; 11·5% was eliminated 1 month after 5 days' exposure and 28% 5 months after similar exposure. One month after 8 days' exposure 12% of the dust was eliminated, and 3·1% had been deposited in the mediastinal lymph nodes; 2 months after the end of exposure 37·4% of the SiO_2 had been eliminated and 10% was present in the lymph nodes.

In the second experiment rats were exposed to Degussa Aerosil in a particle size-range of 10–50 millimicrons and having a 96% SiO_2 content. Exposure was carried out for 7 consecutive daily periods of 6 hours. The mean SiO_2 content 24 hours after the end of exposure was 878 ± 76 μgm.; the regional lymph nodes were enlarged and contained 5 μgm. One month later the mean lung SiO_2 content was 383 ± 45 μgm. *i.e.* 44% of the original value at 24 hours; the lymph nodes were considerably enlarged and contained 34 μgm. *i.e.* 8% of the total SiO_2 recovered. After 3 months the mean lung SiO_2 content was 85 ± 12 μgm. *i.e.* 10% of the 24-hour value and in the even larger lymph glands there was only 25 μgm. *i.e.* 23% of the total recovered. After 5 months the mean lung SiO_2 content was 49 ± 5 μgm., only 5·5% of the 24 hour value, and in the lymph nodes, which were now smaller, there was 14 μgm. *i.e.* 22% of the total recovered.

The results showed quartz dust given in high doses for short periods to be slowly eliminated whereas fine particles of aerosil dust were rapidly eliminated.

D. Rivers

KLOSTERKÖTTER, W. Tierexperimentelle Untersuchungen über die Gewebswirkung von feinkörnigem Gamma-Aluminiumoxyd. [**Investigation of the Tissue Changes Produced by Fine Particles of Gamma-Aluminium Oxide in Animal Experiments**] *Arch. f. Hyg. u. Bakt.* 1959, Feb., v. 143, No. 2, 85–111, 33 figs. [43 refs.]

Gamma-aluminium oxide is a constituent of the fumes to which corundum smelters are exposed and the author considered that it might have fibrogenic qualities.

Pure Al_2O_3 has not been previously tested extensively in experimental animals. Gamma-Al_2O_3 in the particle size range of 0·005–0·04 micron was administered to albino mice in doses of 10 mgm. by intraperitoneal injection. The injections were not well tolerated but the animals recovered normal vitality 3–4 days after injection. Groups of mice were killed at 45, 90, 125 and 150 days after injection. Numerous 0·5–2·0 mm. nodules were seen in the animals killed at the earlier intervals but at 150 days their number was fewer. The dust was well phagocytosed and did not appear to damage the macrophages, around which only a slight reticulin reaction developed.

In the second experiment rats received 50 mgm. gamma-Al_2O_3 by intraperitoneal injection. Groups were killed at 60, 180 and 320 days after injection and the findings were similar to those seen in the mice.

In the third experiment rats received 35 mgm. gamma-Al_2O_3 by intratracheal injection and the animals were killed at 10, 150, 180 and 390 days after injection. Most of the dust was seen to be phagocytosed 10 days after injection and was completely intra-alveolar. After 150 days alveolar walls adjacent to the dust foci were thickened and there was focal emphysema. No animals showed evidence of progressive fibrosis as seen in experimental silicosis.

In a further experiment rats were subjected to a high concentration of gamma-Al_2O_3 in an inhalation chamber. The maximum period of inhalation was 285 days and the animals were observed for a total period of 402 days.

Chemical analysis of the lungs showed considerable variation in retention of aluminium oxide. Thus the amount retained after 8 days in the inhalation chamber varied from 1·6 to 3·8 mgm.; after 10 months' inhalation lung Al_2O_3 content varied from 20·3 to 36·5 mgm.

No quantitative estimates were made of elimination of dust. The animals did not tolerate the dust inhalation well; 107 of the original 145 rats died at numerous intervals during the course of the experiment. The remaining 23, without any evidence of illness, were killed at intervals of 4, 10 and 13 months. The lungs showed numerous white 1 mm. subpleural nodules and the mediastinal lymph glands were considerably enlarged. There was marked desquamation of the alveolar epithelium and there was only a slight reticulin reaction within the dust foci which were also associated with focal emphysema. There was also slight sclerosis of the alveolar walls.

From these experiments the author concludes that gamma-Al_2O_3 only causes fibrosis in extremely high concentrations, whereas small doses cause only slight foreign body reaction without significant damage to the tissue. It is considered unlikely therefore that gamma-Al_2O_3 makes any important contribution to corundum smelters' lung, but the possibility is not excluded.

D. Rivers

MCCORD, C. P. **Metal Fume Fever as an Immunological Disease.** *Indust. Med. & Surgery.* Chicago. 1960, Mar., v. 29, No. 3, 101–7. [13 refs.]

The author describes the illness of metal fume fever in detail with long quotations from other works. He states that for decades the disposition has been to regard metal fume fever as some form of allergy [it

does not appear to be so regarded to any great extent in Britain]. He attempts to explain on a purely theoretical basis the phenomena of metal fume fever on the assumption of dual groups of antibodies with activities in conflict. His reasoning is somewhat obscure and he does not discuss the theory of direct toxic action of the freshly formed fume on the epithelial cells of the respiratory tract resulting in protein shock reaction, the short-lived immunity being due to the accompanying leucocytosis. *A. T. Doig*

ROACH, S. A. & SCHILLING, R. S. F. **A Clinical and Environmental Study of Byssinosis in the Lancashire Cotton Industry.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 1–9, 3 figs. [16 refs.]

This study was undertaken to investigate the differences in the incidence of byssinosis between mills spinning coarse and those spinning fine cotton, and thereby to determine safe levels of dustiness in the atmosphere. The dust was sampled after being passed through a wire gauze which trapped particles over 2 mm. in diameter. This trapped portion of the dust is referred to as coarse; dust passing through the filter is referred to as medium and fine. At the same time samples were drawn through an elutriator which eliminated most of the particles with an equivalent diameter of more than 5 microns, the dust collected on the filter paper behind this elutriator is referred to as fine. These fractions of dust were weighed and analysed for protein and mineral content.

2 groups of mill were studied in which the working conditions were not thought to have changed much in 25 years. In the coarse mills 243 workers in card-, blow- and mixing-rooms and 365 in spinning-rooms were examined, and in the fine mills 172 workers in the carding etc. rooms. Dust samples were taken at the workers' places of work according to the technique described by OLDHAM and ROACH [this *Bulletin*, 1952, v. 27, 938].

Byssinosis was assessed clinically by the technique of SCHILLING [*ibid.*, 1956, v. 31, 1116].

In the coarse mills the prevalence of byssinosis was high in the card-rooms and low in the spinning-rooms, in the mixing- and blow-room workers the prevalence was intermediate. In the fine mills the prevalence of byssinosis was low and confined to the card-room workers. The closer the workers were to the carding engines the higher was the prevalence of byssinosis. Dust concentrations were higher in the coarse than the fine mills, and higher near the carding engines than in other positions in the carding room. Samples on various days of the week showed that, if anything, dust concentrations were lower on Monday than on other days of the week so that the increase of symptoms of byssinosis on Monday was not due to higher dust concentrations on that day.

In all the rooms less than 8% by weight of the dust consisted of fine particles. The coarse dust accounted for 60% or more of the weight of the dust. Most of the coarse dust consisted of cellulose. Medium and fine dust contained higher proportions of protein and minerals, the proportion of cellulose being least and the proportion of minerals being highest in the fine dust. In order to relate the prevalence of byssinosis to dust concentration, 10 groups of workers who had spent 95% or more of their working days in one room or pair of rooms were separated, and correlation coefficients between the dust concentrations in these rooms and the prevalence of byssinosis in each group were estimated.

Partial correlations were calculated for each constituent of the dust and for each size fraction of protein dust. These correlations were as follows:—

	Total Correlation	Partial Correlation
Total dust	0·93	–
All cellulose	0·81	0·58
All protein	0·94	0·90
All ash	0·58	−0·40
Fine protein	0·58	0·03
Medium protein	0·95	0·55
Coarse protein	0·93	0·14

The correlations suggest that the protein component, and especially the medium size fraction are most closely associated with the prevalence of byssinosis.

Since the correlation between the prevalence of byssinosis and total dust is close it is suggested that total dust concentrations should be used for expressing maximum permissible levels of dustiness. In a table showing the relationship between concentration of dust, duration of exposure and prevalence of disease it is shown that only those workers exposed to a concentration of less than 100 milligrams per 100 m^3 were free from byssinosis, so that this can be regarded as a safe level. Between 100 and 250 milligrams per 100 m^3 dust control is desirable and medical supervision essential. At higher levels both dust control and medical supervision are essential. Medical supervision is in any case desirable because there may be hitherto unsuspected harmful fractions of the dust that might be present even in the absence of high total dust concentrations. *C. M. Fletcher*

LOGAN, J. S. **Flax-Dust Byssinosis and Chronic Non-Tuberculous Chest Disease in Belfast.** *Ulster Med. J.* 1959, Nov. 1, v. 28, No. 2, 164–75. [26 refs.]

Flax byssinosis occurring among workers in the flax and linen mills around Belfast has been recognized by Ulster physicians. The author describes 10 hospital patients with this disease which is said to be commonest among the hacklers who prepare the flax for spinning. Both hackling and the carding of tow are very dusty jobs. The clinical history is similar to that of byssinosis of cotton workers. There is chest tightness, breathlessness and cough on Mondays which, as the disease progresses, occur on other days. All the patients described were under 58 years of age. 3 apparently died of byssinosis and others were severely disabled by it. In Belfast it is quite a common disease

easily recognized in its grosser forms by the occupational history, the Monday exacerbations of chest tightness and lack of characteristic radiographic changes in the lung fields.

At present, flax byssinosis is not a prescribed disease. Therefore, neither disablement nor death benefit is payable. One of the patients in this series did make a successful claim against his employer at common law. The author emphasizes that his observations are based on hospital patients and that knowledge of this disease, its incidence and severity could best be advanced by surveys in industry. *R. S. F. Schilling*

ANN. OCCUP. HYG. London. 1959, Dec., v. 2, No. 1, 1–84, numerous figs. [19 refs.] **The Control of Dust and Fume in Industry.**

This symposium comprises papers presented at the Tenth Conference of the British Occupational Hygiene Society held at Sheffield on 14th and 15th April, 1959. After each paper an account is given of the discussion which followed it.

T. W. MCCULLOUGH. *Introductory Paper* (pp. 1–5).

The early steps in dust suppression in factories are reviewed from 1903, when regulations were made dealing with the risk of lead poisoning in file cutting, to the present day. The basic principles of dust control are discussed.

F. BROWNSETT. *Dust in Card-rooms* (pp. 6–15).

After a brief description of the components of card-room dust, and methods used to measure the dust concentrations (surprisingly he says . . . " in general there is no correlation between the results obtained by the different methods "), the author describes in some detail methods of reducing dust exposure under five headings: (1) Cleaning the cotton before it enters the card-room. Much dust and trash may be removed but a limiting factor is the necessity of avoiding damage to the fibre. (2) Provision of respirators. These vary in efficiency. Resinated wool masks may have an efficiency of about 88%; a commercial cotton mask was shown to remove 42% of the dust but this was chiefly cotton fly rather than fine dust. (3) General ventilation of the workroom. A large volume of air is required to be removed to give any significant dust removal, and this leads to substantial heat loss. (4) Oiling of cotton. Owing to several disadvantages, this has been largely given up. (5) Local exhaust ventilation. This is the best method and the Pressure Point System designed by the Shirley Institute is described in some detail. The method makes use of high pressure zones and deflectors to concentrate airflow at certain points, thus reducing the airflow speed necessary to remove dust. Tests showed an efficiency between 84 and 94% with an airflow of 250 cu.ft./minute per card. Several mills are now equipped with this apparatus which appears to be giving considerable satisfaction.

G. MACBAIN. *Methodology in the X-Ray Study of Pneumoconiosis in the Ironfounder* (pp. 16–29).

The scheme for X-ray supervision of workers which is in operation at one firm is described in detail. Although it is voluntary the first survey obtained a 98% response from the 5,000 employees. The results of this survey are not given in detail but the author has found cases of pneumoconiosis in comparatively young men, several of whom had had less than 10 years' service. He discusses the use to which this information has been put in regard to reducing the risk. He advises careful supervision of jobs of known risk, with rigid compliance of legal requirements, regular maintenance and testing of plant, assessment of air contamination (the Hexhlet apparatus is used), chemical analysis of dusts, good general ventilation and localized exhaust ventilation where possible. The author sees little hope of making foundries 100% safe in the foreseeable future, but by X-ray supervision cases can be detected at a stage before there is disability and when there is little likelihood of progression if further dust exposure is prevented.

H. W. HURLEY. *The Control of Fumes in the Electroplating Industry* (pp. 30–38).

The removal of fumes from chromium and other electroplating tanks, cleaning and pickling tanks, and of dust in polishing departments is discussed.

G. H. VOKES. *Air Conservation in Industry* (pp. 39–53).

The author points out the feasibility of internal recirculation of air from dusty processes after adequate dust removal. He examines objections to recirculation and disposes of them by saying that with modern, high efficiency methods of filtration, recirculated air can be as clean, frequently cleaner, than air outside the factory. He admits that a breakdown is possible, but states that he would never advocate recirculation of air from conventional bag filters as these might be torn or become dislodged, and that dust filtration and collecting equipment should be regularly inspected and maintained. He goes into the question of heating costs to show that recirculation would effect a considerable financial saving, and he makes out a very strong case for recirculation where dusts of limited toxicity are encountered except when concentrations are excessive.

W. P. BAMBLIN. *Dust Control in the Asbestos Textile Industry* (pp. 54–74).

After giving a vivid account of conditions in this industry prior to 1930, the author describes in detail modern methods of dust suppression as applied to various machines used in the asbestos textile industry. Dust counts are taken once monthly as a routine at a number of sampling points throughout the works by using the standard thermal precipitator, and also the Ottway Long Running Thermal Precipitator. No results of air sampling are given, but it is stated that of 398 persons employed for 10 years or more since 1933 (the date when preventive measures can be said to have been effectively established) only 3 have been suspended for asbestosis by the Pneumoconiosis Medical Panel, and all 3 are still employed although on other work.

J. W. ROE. *Gases and Fumes Produced in Fusion Welding and Cutting* (pp. 75–84).

This is largely a summary of available information on the gases and fumes evolved in welding processes

with a brief chapter on control. A series of illustrations shows very clearly the necessity of having the local exhaust hood close to the arc and the effectiveness of providing it with a flange. *A. T. Doig*

KLINE, Tilde S. **Myocardial Changes in Lead Poisoning.** *J. Dis. Children.* Chicago. 1960, Jan., v. 99, No. 1, 48–54, 5 figs. [12 refs.]

Symptoms of palpitation, dyspnoea and precordial discomfort in patients with chronic lead poisoning have been mentioned briefly in the literature since 1829. The term "angina pectoris saturnina" was coined in 1926 for such conditions, which were thought to be due to spasm of the coronary vessels. Sporadic cases have been described since that time.

In a recent fatal case of acute lead poisoning in a 2-year-old child, complete autopsy was performed and changes in the myocardium characteristic of subacute interstitial myocarditis were found. There are 5 photographs of the microscopical findings. Previous autopsy records were then reviewed and disclosed myocardial changes in 4 more children who had suffered from lead poisoning. There are case reports of these children in which the most essential clinical and autopsy findings are given.

In summary, "autopsy evidence of lead encephalopathy was found in all, in addition to chronic myocarditis". It is recommended that in cases of lead poisoning "Routine electrocardiographic studies and close scrutiny for possible clinical evidence of myocardial damage" should be carried out.

M. E. Delafield

EMMERSON, B. T. & THIELE, B. R. **Calcium Versenate in the Diagnosis of Chronic Lead Nephropathy.** *Med. J. Australia.* 1960, Feb. 13, v. 1, No. 7, 243–8, 2 figs. [19 refs.]

In much of the chronic renal disease in Queensland, the incidence of which is greater than in other Australian states [this *Bulletin*, 1934, v. 9, 43; 1940, v. 15, 71] lead poisoning in childhood from ingestion of lead-containing paint has been accepted as the major aetiological factor. All the reported investigations on this subject, however, have "revealed the difficulty of deciding incontrovertibly during life whether, in a particular case of chronic renal disease, the lesion was due to childhood lead poisoning or to other factors".

In this paper there is a detailed account of the methods of investigation undertaken to determine the urinary lead excretion after the intravenous injection of calcium versenate in 9 patients with nephropathy and 1 who had had lead poisoning in childhood but had no renal lesion. There were 6 normal control subjects. The results of the study are described and discussed fully with tables and figures. It was found that increased and prolonged urinary lead excretion followed on intravenous infusion of 1·0 gm. of calcium disodium versenate in "some patients with advanced renal disease due to childhood lead poisoning who had had no appreciable exposure to lead for periods of up to forty years". It is suggested that infusion of versenate may be of value in the diagnosis of chronic lead nephropathy.

M. E. Delafield

ROCHE, L., BADINAND, A. & LEJEUNE, E. Les chélateurs dans le saturnisme. [**Chelating Agents in Lead Poisoning**] *Arch. Malad. Professionnelles.* Paris. 1960, Jan.–Feb., v. 21, Nos. 1/2, 1–12, 3 figs.

Infusions of EDTA in 250 ml. of *sérum glucosé isotonique,* the injections taking at least 2 hours, were well tolerated during the management of 29 overt or suspected cases of lead poisoning. Tolerance was tested with 0·5 gm. EDTA in the solution. Afterwards 2 infusions a day each containing 0·5–1 gm. were given for 2–4 days to establish diagnosis or for 7–10 days therapeutically. Therapeutic courses were repeated at monthly intervals or longer.

Clinical signs of lead poisoning together with significant amounts of stippling, urinary lead and coproporphyrinuria were present before chelation in 6 cases of occupational and 2 of accidental poisoning, but in the remainder symptoms and results of tests were uncharacteristic or inconclusive, though many patients had been exposed to lead in their work. Graphs and tables show, among other details, the 24-hour urinary lead contents before and after chelation. Based on the contents mobilized by chelation, the 21 debatable cases were divided into 3 groups, with more than 2,000 μgm., 800–2,000 μgm. and less than 800 μgm. lead in a mean daily urine volume of about 2,200 litres, diuresis having been caused by the infusions. The contents in the first and second groups were pathological, the first representing a high degree of impregnation associated with clinical manifestations, present or imminent, the second, moderate storage with, occasionally, symptoms. The third group was not more at risk than was the general community.

The patients with lead poisoning improved with the therapy except those with nephritis in which however the aetiology was established by chelation. In a case of arsenical neuritis from lead arsenate the induced urinary lead reached 1,884 μgm. Tissue contents are given for a patient with lead neuritis who died of cardiac disease 3 months after completing 3 courses.

In diagnosis this method was of value in assessing latent cases, in overcoming the difficulty of marginal laboratory findings and in making it possible to exclude lead poisoning in ambiguous cases.

M. Patricia Fitzsimons

KÜHNEN, G. Bestimmung von Blei in Luft. [**Determination of Lead in Air**] *Staub.* Düsseldorf. 1960, Mar. 1, v. 20, No. 3, 77–81, 1 fig. [10 refs.]

Although the amount of industrial lead poisoning has lessened greatly in the last decades it remains necessary to control the actual amount of suspended lead dust in the atmosphere of work rooms in some industries. There is in this paper some discussion of the methods which may be employed for the determination of the concentration of suspended lead and of the accuracy of these methods.

There is a full account of a method developed by the author in which there is a description, with a diagram, of an apparatus for obtaining by filtration the dust contained in a measured volume of air. The chemical analysis of determination of lead is carried out by a dithizone method which is also described in detail and is claimed to be time saving because purification of the reagents is unnecessary.

Some experimental results with the method indicate that it may be used for determining amounts of lead in a range of 10 to 120 μgm. with an average accuracy of 1·0%. *M. E. Delafield*

Borbély, F. Die Quecksilbervergiftung. [**Mercury Poisoning**] *Ztschr. f. Unfallmed. u. Berufskrankh.* 1960, Mar. 15, v. 53, No. 1, 31–53. [Numerous refs.]

A general review of the subject.

Dinman, B. D. **Arsenic: Chronic Human Intoxication.** *J. Occup. Med.* Chicago. 1960, Mar., v. 2, No. 3, 137–41. [34 refs.]

Ritter, J. & Marti Feced, C. Essais et résultats du traitement des manganiques et de la prophylaxie de l'intoxication manganique par l'E.D.T.A. Ca ou calcitétracémate disodique. [**Investigations of the Value of EDTA in the Treatment and Prevention of Manganese Poisoning**] *Arch. Malad. Professionnelles.* Paris. 1960, Mar., v. 21, No. 3, 115–30.

Some description of the composition, chelating action and use in lead poisoning of EDTA (calcium disodium versenate) precedes this account of its employment in the treatment and prevention of manganese poisoning in 2 mines in Southern Morocco. In this paper clinical observations on manganese intoxications are not described as these were reported in a previous publication.

The method of therapy adopted in 1 of the mines was to give 5 courses of treatment, each 5 days in length at an interval of 1 week between courses for the first 3, and 15 days between the fourth and fifth courses. EDTA was given intravenously in a daily dose of 1·0 gm. dissolved in 500 cc. of isotonic glucose saline, half of which was given in the morning and the other half at night. The dose was increased to 2·0 gm. daily for the second and third and to 3·0 gm. for the fourth and fifth courses. The results are described with tables of particulars of blood counts. The main conclusions were that EDTA administered in definitely established manganese poisoning produces no amelioration but appears to arrest the condition. When used in early cases in which there are mainly subjective symptoms EDTA treatment results in a spectacular regression of all symptoms.

As a prophylactic EDTA was given to a number of miners in a daily dose by mouth of 0·5 gm. for 5 days in each week. The results were very encouraging since the miners have remained free of any signs of manganese intoxication throughout the 23 months of observation. *M. E. Delafield*

Csillag, S. & Hochenburger, E. Gyári dolgozók fül-orr-gégészeti szürövizsgálatai kapcsán nyert tapasztalataink, különös tekintettel a chromártalomra. [**Results of an Otorhinolaryngological Investigation of Factory Workers, with Particular Regard to Chromium Poisoning**] *Népegészségügy.* Budapest. 1959, July, v. 40, No. 7, 177–80. [Numerous refs.]

The authors have carried out a clinical investigation of 35 persons working in a chromium plating shop. One worker who had been exposed to chromic acid vapour for many years was found to have a perforation of the nasal septum, and in 7 others a grey patch was observed on the anterior part of the nasal septum. In an investigation of 285 workers in the same factory 87 (27%) were found to have some abnormal condition of the ear, nose or throat, requiring operative treatment (resection of septum, nasal polyp, laryngeal papilloma). *D. J. Bauer*

Darabos, L. & Mohos, J. Z. A magyar cementek bichromát-tartalma. [**The Dichromate Content of Hungarian Cements**] *Népegészségügy.* Budapest. 1959, July, v. 40, No. 7, 180–83. [18 refs.]

The authors have investigated the dichromate contents of samples of raw material and final products from 6 Hungarian cement works. The cement from one works contained 0·3–3·0 mgm.% chromium as dichromate, and contents of 0·3–0·9, 0·3, 0·02–0·04 and 0·1 mgm.% were found in samples from 4 other works. No dichromate could be found in the raw materials. Attention is drawn to the risk of sensitization in persons constantly using cement with a high dichromate content. *D. J. Bauer*

Paolino, W. & Vercellino, E. **Effects of Adenine on Blood Disease due to Benzene Poisoning.** *Panminerva Med.* Turin. 1960, Jan., v. 2, No. 1, 5–8. [Translation from *Gazz. Med. Italiana*, 1959, v. 118, 18.]

Sub-acute poisoning was caused in 5 groups of rabbits by intramuscular injection of 1 ml. per kgm. 40% benzene solution on alternate days until death. Adenine was not given to 1 group, the controls. In 2 groups it was given from the start by daily intramuscular injections of 6 or 30 mgm. respectively, and in 2 others these doses were started only when the leucocytes had decreased to one-third of the initial counts.

With the exception of the group given 30 mgm. adenine throughout, reticulocyte responses, white cell counts and marrow biopsies were similar, and in all 5 groups survival times were about 1 month, and platelets were unaffected. The adenine did not modify the fall in haemoglobin and in erythrocytes.

With the large protective dose there were these differences. The early leucopenia was slight and just

before death the total number of leucocytes averaged 7,500 (controls 2,050). Neutrophils remained for some time at the initial level, 3,600, and fell terminally to 2,275 (control averages 1,000 and 399). Reticulocytes fell rapidly. The 3-fold increase of reticulocytes observed in the other 4 groups for 15 days before the decrease was considered a sign of the marrow disorder: weekly biopsies showed a decrease in cells, a relative increase of the lymphocytic ratio and a decrease of the leuco-erythrogenetic ratio because of the reduction of granuloblasts. In the protected group, there were more nucleated cells, especially granuloblasts, and the leuco-erythrogenetic ratio showed a smaller drop.

Adenine had shown some effect on the leucopenia occurring during treatment with diacetylcolchicine. The authors suggest that it would be worth while testing the effect of large doses of adenine, identified as vitamin B4 and the active principle of pentose-nucleotide, in the leucopenia of chronic benzene poisoning.

M. Patricia Fitzsimons

GERARDE, H. W. **The Toxicology and Biochemistry of the Monc-Cyclic Aromatic Hydrocarbons.** *Med. Bull.* New Jersey. 1960, Mar., v. 20, No. 1, 74–90, 26 figs.

This review of the author's 5 years' research presents conclusions derived from studies of 50 alkyl derivatives of benzene, the phenylalkanes [this *Bulletin*, 1959, v. 34, 910]. They are used as solvents for paints, plastics, pesticides and protective coatings, as constituents of petrols and in chemical syntheses. They differ from benzene, a neurotoxic convulsant and a blood-damaging poison. Structural formulae and models of molecules show the variety of structure. Toxicity and nervous depressant activity of the mono-*n*-alkylbenzenes decrease with chain length beyond 2 carbons. Toxicity is decreased by multiple alkylation and increased by chain branching and unsaturation. Alkylbenzenes are more irritating than benzene, but they do not damage blood forming tissues.

This absence of myelotoxic effect was demonstrated by serial examinations of groups of rats killed during exposures and for 3 weeks after; they were subcutaneously injected with 10 ml. per kgm. daily for 2 weeks. Graphs of mean values in controls and in rats dosed with alkylbenzene and benzene show the first 2 groups to be alike in weight, white cell counts and marrow nucleated cell counts while the benzene group had low values. The haematocrit was unaffected in the benzene group. Photographs show a small rat, a small thymus and a large spleen after benzene beside a normal-sized rat, thymus and spleen after alkylbenzene, and also test tubes containing normal femoral marrow after alkylbenzene and the fluid, bloody marrow after benzene. Marrow, thymus and spleen however became normal at the end.

Diagrams of metabolism and excretion after oral isopropyl benzene and benzene show 90% of the former excreted in the urine as metabolites and 40% of the benzene as phenolic compounds. These caused darkening of femoral cartilages and, after exposure to light, of urine; both effects are shown in photographs. Photographs also demonstrate a colour change in rats dosed with the ortho- and meta-isomers of diethylbenzene, but not with the para-isomer; the blue metabolite is not yet identified. Alkylbenzenes are mainly excreted in the urine as conjugated alcohols and carboxylic acids formed by oxidation of the alkyl group, the ring not being affected.

M. Patricia Fitzsimons

RUBINO, G. F.; SCANSETTI, G.; TROMPEO, G.; GAIDO, P. C. Studio sull'intossicazione cronica da trielina. Nota 2ª. Assorbimento del tricloroetilene [RUBINO, SCANSETTI & TROMPEO]. [**Studies on Chronic Trichlorethylene Poisoning. II. Absorption of Trichlcrethylene**] *Med. d. Lavoro.* 1959, Dec., v. 50, No. 12, 733–42, 6 graphs. English summary. Nota 3ª. Metabolismo del tricloroetilene [SCANSETTI, RUBINO & TROMPEO]. [**III. Metabolism of Trichlorethylene**] *Ibid.*, 743–54, 4 graphs. [17 refs.] English summary. Nota 4ª. Il catabolismo dei derivati del tricloroetilene [RUBINO, SCANSETTI, TROMPEO & GAIDO]. [**IV. Catabolism of Trichlorethylene Derivates**] *Ibid.*, 755–65, 4 graphs. [24 refs.] English summary.

II. The authors have carried out investigations in 33 dry cleaning establishments and studied the relationship between occupational exposure to trichlorethylene vapour, the rate at which the workers absorb it into their system and the ultimate fate of the chemical. The observations were made on 31 of the 41 subjects employed. The operations of treating the clothes with the solvent and of pressing them were carried out in the same room. The authors describe their technique and tabulate their findings—maxima of 0·05–2·00 mgm./litre trichlorethylene in the working atmosphere and concentrations of 0·1–0·83 mgm./100 cc. in the workers' blood. The tables include information about the age, the task of each worker and the number of years for which he has been exposed to the hazard.

There was only a slow disappearance of the chemical from the blood after removal from exposure: the concentration had dropped by about half in 2 days.

Trichlorethylene is a general anaesthetic and its absorption and elimination was studied in a 20-year-old youth who was given 2·5 cc. by inhalation in 10 minutes: more than half the amount inhaled had reached the blood plasma at the end of the 10 minutes and half the quantity so absorbed had been excreted by the end of 42 minutes.

At Naples in 1954 the International Union of Pure and Applied Chemistry accepted a maximum permissible concentration of 100 p.p.m.; the Clinica del Lavoro, Milan, has laid down 200 p.p.m. as a limit [PARMEGGIANI, this *Bulletin*, 1956, v. 31, 1228]. The atmosphere in 11 of these establishments exceeded the former figure and in 3 the latter.

III. 30% of trichlorethylene which is inhaled is at once got rid of in the breath. When a single massive dose of the vapour is taken, exhalation from the lungs ceases after about one hour, the rest being carried by the blood stream to various tissues—subcutaneous and other fat, adrenals, ovaries, brain, spleen and liver—

where it is stored. In due course, blood and urine show the degradation products of the chemical.

The authors of this paper report on the metabolism of trichlorethylene as they observed it in 31 employees of dry cleaning establishments. They estimated the concentrations of its breakdown products in the blood serum, and give graphs and tables of their findings. They found trichloracetic acid, free and combined trichlorethanol, chloral hydrate and residues of unchanged trichlorethylene in the samples of blood. The products are the result of intracellular metabolic processes which develop at a slow rate and may involve some cycles with reabsorption.

IV. Whether trichlorethylene is inhaled as a single massive dose or absorbed over a period from the occupational atmosphere, the chloral hydrate which results from its metabolism has a short half-life in the blood stream. Trichlorethanol persists for much longer in the blood serum and can be found 15 days after a single inhalation. Trichloracetic acid is the last of these metabolites to appear in the blood serum ; after a single massive inhalation of the anaesthetic the metabolite takes 50 hours to reach maximum concentration, may persist for a fortnight and has the longest half-life.

In the present paper the authors report on the concentrations of these breakdown products in the urine of 31 employees working in dry cleaning establishments: the urine samples were taken at the end (Friday) of a working week's exposure to the hazard and then again 48-72 hours later. The authors give an account of their technique and they tabulate and plot their findings, expressing their results in mgm./100 cc. and mgm./hour. They have found a direct correlation between the concentration of trichloracetic acid in the blood serum and its rate of excretion with the urine. This rate is much faster after a single massive dose than after long-continued occupational absorption. They have found no similar correlation of the rate of excretion of trichloracetic acid in the urine with the content of trichlorethylene in either the working environment or in the blood. On the other hand, the concentration of total, *i.e.* both free and combined, trichlorethanol in the urine and in the blood is a measure of the trichlorethylene which has been absorbed and, therefore, of its concentration in the working atmosphere. The slow rate of clearance after industrial poisoning is partly explained by the strong combinations of these breakdown products with protein elements of blood and cells. *J. Cauchi*

RUIKKA, I. **Postprandial Serum Turbidity in Chronic Carbon Disulphide Poisoning. A Comparison of Viscose Rayon Workers with Healthy and Atherosclerotic Men.** *Ann. Med. Intern. Fenniae.* Helsinki. 1959, v. 48, Suppl. 31, 92 pp., 4 figs. [Numerous refs.]

These studies were undertaken to see whether lipid metabolism disturbances of the kind associated with atherosclerosis could be used as criteria in the diagnosis and control of chronic CS_2 poisoning. An account of the latter disease includes descriptions of blood vessel lesions and blood lipid abnormalities. Then, serum turbidity following a fatty meal, chylomicron counts and the influence of fat absorption and transport, clearing of turbidity by heparin, serum turbidity during fasting in certain diseases and the postprandial serum turbidity test are all reviewed, and also the results of such tests in atherosclerosis. These have often been contradictory.

In presenting the problem, in the form of questions to which answers were sought in these investigations, it is pointed out that in atherosclerotic patients, among other lipid metabolism disturbances, a slow clearing of the plasma after a fatty meal is a typical phenomenon, and that a greater than normal proportion of atherosclerotics have been reported among groups of patients suffering from chronic CS_2 poisoning.

In describing methods the reasons for them are argued and also the problems of variables. The length of observation time in the main investigation is stressed.

For the main investigation, outlined in the title of this monograph, photometric measurements were made of the turbidity of serum specimens taken immediately before and, at 2-hour intervals, for 8 hours after a standardized meal. This, in which the carbohydrate content was also constant, contained 80 gm. of fat, an amount larger than that given by previous investigators. All other food was forbidden for 8 hours, by which time serum from normal subjects reached fasting level. The rate of clearing was determined in viscose workers who had been exposed to CS_2 for less than 5 years or longer and in those with chronic poisoning, in young trade-school pupils and in hospital in-patients who were recovering from coronary thrombosis—in all 295 ambulatory men.

In the pupils and workers exposed for the short period, the mean turbidity fell back to fasting levels 8 hours after the meal. In workers exposed longer, clearing was retarded, and the 6- and 8-hour increases in turbidity were significantly higher than those of the 2 preceding groups. These values were still greater in poisoned workers and highest of all in the coronary disease group.

Individual serial values, shown in tables in 10-year age bands, varied in all groups. Periods of exposure to CS_2 and work locations in the factory are also given. No differences due to age were found among the workers, aged 21-60. The variability shows that a high postprandial serum turbidity is not a specific measure of exposure, though it is a complementary diagnostic finding. Low values do not rule out the possibility of exposure because absorption may be at fault. High values confirm the diagnosis of poisoning provided atherosclerosis, diabetes, nephrosis, hypothyroidism, etc., are excluded.

The 8-hour value is the most telling, and the fact that the high values in poisoning became lower after removal from exposure is also useful in diagnosis.

Several other investigations were made in workers with chronic poisoning and controls of the same age. The mean serum cholesterol was significantly higher in the former, 287 mgm. per 100 ml. as against 257. The mean beta-lipoprotein percentages were 80% and 75·2% respectively, a significant difference. No differences were found in the mean total protein, electrophoretic protein fractions and lipid phosphorus levels. In the group with poisoning, there was high correlation between beta-lipoprotein percentages and 8-hour turbidity values.

Experiments to study the mechanism of CS_2 poisoning by *in vitro* tests in which an *in vivo* clearing factor

induced with heparin was used, gave no conclusive results. In these tests, clearing of a mixture of cocoanut oil emulsion and albumin was arrested when the clearing factor had been treated with 1 mgm. CS_2 per ml. 24 hours previously. Only a slight arrest occurred when CS_2 was added to the albumin. However, it was recognised that heparin possibly has no part in physiological postprandial clearing.

The results of the main study and the cholesterol levels and beta-lipoprotein percentages indicate that disturbances in lipid metabolism in chronic CS_2 poisoning are similar to those associated with atherosclerosis, and support the view that prolonged exposure to CS_2 may induce or accelerate atherosclerosis in viscose workers, On the other hand, they could point to the possibility of there being in some cases of atherosclerosis, an aetiological factor other than diet. [An errata slip appears at the end.]

M. Patricia Fitzsimons

MUNN, A. **Experiences with Diisocyanates.** *Trans. Ass. Indust. Med. Officers.* 1960, Jan., v. 9, No. 4, 134–8. [11 refs.]

Some years' experience did not prevent illness in a new well designed plant for the large scale manufacture of toluylene 2:4 diisocyanate (TDI). The hazard from these lachrymators which are respiratory irritants and sensitizers, and only rarely skin irritants, was recognized, but not at first its exact significance. Diisocyanatodiphenyl methane (MDI) caused no trouble, except once when perhaps contaminated with TDI, but it is steam volatile and this could constitute a hazard.

Intermittent chest complaints, more common among fitters and labourers than process operators, led to a certain degree of phobia. It was the suddenness of asthmatical symptoms which caused apprehension. Generally, however, onset was gradual, with tightness in the chest and nocturnal cough. Some men had marked dyspnoea with bronchospasm, widespread rhonchi and pyrexia. There was no permanent damage. Eosinophilia occasionally was present.

Steps to avoid physical and psychological illness were successful. The unscientific approach of knocking out walls, to permit greater air movement, instead of depending on the powerful exhaust fans, was popular with the men. Local exhaust systems were made more powerful to prevent deposit of polymer. Spills were decontaminated with a mixture of 50% methanol, 45% water and 4% ammonia liquor. Decontamination of closed vessels and pipes was attempted before opening, and other maintenance safety measures included portable draught ventilation systems and respirators.

Though magnitude of exposure and severity of symptoms are not always proportional, this is no reason for not carrying out routine atmospheric estimations—several times daily where necessary. The apparatus was simple to use and measured concentrations of 0·05–0·2 p.p.m. The maximum allowable concentration (MAC) of 0·1 p.p.m. TDI is considered too high: the odour can be detected between 0·1 and 0·2 p.p.m. [see this *Bulletin*, 1960, v. 35, 117]. Selection of workers took account of those likely to make trivial complaints as well as of respiratory disease and allergy. The tendency to mass suggestion of symptoms among men exposed to diisocyanates exists, but only develops following genuine cases. With appropriate precautions, the increasingly used diisocyanates can be employed with safety.

M. Patricia Fitzsimons

LONDON, Micaela. L'action du superphosphate sur la cholinesthérase sanguine. [**The Effect of Superphosphate on Blood Cholinesterase**] *Arch. Malad. Professionnelles.* Paris. 1960, Jan.–Feb., v. 21, Nos. 1/2, 24–32. [17 refs.]

Since in experimental toxicity work the harmfulness of superphosphate has been shown to be due to its content of fluorides, and the fluorine ion to inhibit cholinesterase *in vitro*, the action of superphosphate on rabbit blood cholinesterase was compared, *in vivo* and *in vitro*, with that of sodium fluoride. Solutions of the chemicals containing equivalent amounts of fluorine were used. A colorimetric method for estimating cholinesterase activity in human blood was modified for the rabbit, and the results of the method were verified by tests with eserine in controls and also by means of dorsal muscle contraction in the leech.

Blood samples from rabbits were measured for activity, then mixed with solutions (190 μ F per 0·1 ml.) and tested again 30 minutes later. Acute poisoning was effected by intragastric intubation of solutions, in doses of 4 gm. per kgm. superphosphate or of 99 mgm. per kgm. sodium fluoride. Overwhelming poisoning, lethal in 2 hours, was effected with larger doses and the fluoride was injected intravenously into yet other animals. Blood samples were taken before and up to 2 hours after poisoning and also in the acute poisoning experiments on each day until death, 2-3 days later. Tables show several individual serial cholinesterase activities before and after each experiment.

The results show that the action of superphosphate *in vivo* is different from its action *in vitro*. It was strongly inhibitory *in vitro* in proportion to concentration, 52% when 0·1 ml. superphosphate solution was added and 91% with 0·2 ml. However, there was no cholinesterase inhibition from acute or overwhelming poisoning by either chemical. It is possible that chronic poisoning, which would simulate industrial exposure, would give more information.

M. Patricia Fitzsimons

MCLEAN, E. M. **An Investigation into the Occurrence of a Specific Dermatitis in Native Mine-Workers in the Orange Free State.** *Proc. Mine Med. Officers' Ass.* Johannesburg. 1959, July–Sept., v. 39, No. 370, 41–7, 7 figs. Discussion 47–8.

Considerable disability resulted from a dermatitis of the extremities affecting mainly underground workers in a group of mines in the Orange Free State. It was known locally as "Water Rash".

The only symptom was itching, which was followed by a rash which was first macular and then vesicular. The vesicle ruptured and became secondarily infected

and the last stage consisted of healing, leaving a dry skin with an exfoliating horny layer. Not only the feet, but occasionally the scalp, ear and axilla were involved. The histology was characteristic of an eczematous condition.

During the year 1955, 189 cases were admitted to hospital, approximately 50% of all cases seen, out of a total of 25,000 labourers.

After extensive investigation it was believed that the trouble was due to working in a humid atmosphere associated with contact with an alkaline water aggravated by local trauma and sweating. The use of boracic powder on the feet and the wearing of thick woollen socks reduced the incidence. A variety of local applications were used in treatment, including hydrocortisone ointment. An early application of 10% salicylic acid in 90% alcohol appeared to hasten the process of desquamation and shorten the duration of the illness if used in the early stages, but where the condition was advanced no specific remedy was found.

H. T. H. Wilson

BUCKLEY, W. R. & NORRIS, J. L. **Dermatitis in a Chemical Industry.** *J. Occupational Med.* Chicago. 1959, June, v. 1, No. 6, 333–8.

Skin disorders referred to a dermatologist over a 4-year period are tabulated. They represent cases coming from a total of some 33,000 employees. Of the total 26% were occupational, 83% of these patients being males and 17% females. Non-occupational diseases accounted for 74%, 75% of the patients being males and 25% females.

The occupational group included the diseases due to contact with external agents, both sensitizers and primary irritants, excessive drying of the skin and aggravation of a pre-existing condition such as psoriasis. Other causes were folliculitis from cutting oils, thermal burns, traumatic and infective conditions. Drug sensitivity accounted for some cases and a few new growths were attributed to exposure to light in the course of occupation. A miscellaneous group included argyria and miliaria.

In the non-occupational group infective conditions, mainly due to fungi, viruses and bacteria, presented a most important problem. Other conditions included non-occupational contact dermatitis, disorders of the sebaceous glands, eczema, neurodermatitis, congenital diseases, new growths, urticaria and diseases due to trauma, physical agents and disturbances of pigmentation.

H. T. H. Wilson

FABRE, R. Sur les propriétés toxicologiques des constituants des pétroles. [**Toxic Effects of Petroleum Products**] *Arch. Malad. Professionnelles.* Paris. 1960, Mar., v. 21, No. 3, 97–106.

This paper contains some account of the toxic action on man and animals of some of the constituents of petroleum products such as pentane, hexane, heptane, octane and benzene. Particular mention is made of the skin diseases which may result from contact with a variety of petroleum products. In a recent study of 1,000 cases of occupational dermatitis in the Paris region, 168 were in men who had been in contact with these products. There were 133 cases of oil acne (*bouton d'huile*) and of these 118 were due to cutting oils (*huiles de coupe*), to which sulphur and chlorine compounds of various kinds have been added by the makers to make them suitable for use in high-speed machines.

M. E. Delafield

HEATING, LIGHTING AND VENTILATION

SMALL, B. R. **Factory Heat Waves can be Broken.** *Amer. Indust. Hyg. Ass. J.* 1960, Feb., v. 21, No. 1, 32–8, 5 figs.

The author discusses methods of reducing heat stress in hot industries without using refrigeration as the source of cooling. First he refers to ventilative cooling, in which large volumes of outdoor air are drawn into the factory and so discharged as to produce the cooling effect where it is wanted. Cooling by the local delivery of cool air may not be adequate in places where there is much radiant heat, as in the neighbourhood of furnaces. Then the radical treatment is to provide suitable reflective shields so as to screen the operatives from the radiant heat. The combination of radiation shields with ventilative cooling can be of great value.

In some situations evaporative cooling can give much relief. The ventilating air is passed through a water-spray chamber and thus cooled before being discharged only a few feet from the workers. It is pointed out, however, that this method is of only limited application except in hot, dry localities.

Examples of the application of these methods are described.

Thomas Bedford

ANGUS, T. C. **The Effects of Mechanical Ventilation on Airborne Bacteria.** *Med. Press.* 1960, Mar. 9, v. 243, No. 10, 214–16, 1 fig.

The author and a colleague estimated the effects of mechanical ventilation on the concentrations of bacteria in the air of an occupied lecture room, and in the present paper the possible significance of the results in relation to the ventilation of operating theatres is discussed.

The experiments were carried out on 5 days. In the first experiment the room was closed, and there was no ventilation except a small amount of infiltration. On the remaining days the ventilating plant supplied air at

the rate of about 26 cu. ft. a minute for each person. In one experiment the whole of the air supplied was fresh air from outdoors. In another there was no fresh air and all the supply air was drawn from the room itself. In the other two experiments respectively 4·8 and 13·4 cu. ft. per minute of the air supplied per person was fresh air and the remainder was room air recirculated.

When the fans supplied only recirculated air the bacterial count was 23 bacteria per cu. ft., while when the mechanical plant was not used there was a count of 43 bacteria per cu. ft. When the whole of the air supplied by the fans was drawn from outside the count was 19 bacteria per cu. ft., and on the days with partial recirculation the counts were 25 and 22 bacteria per cu. ft. when the supply of fresh outdoor air was 4·8 or 13·4 cu. ft. per minute respectively. On the days when the ventilating plant was running there was no great difference between the bacterial counts, and those counts were substantially less than when the plant was not used.

It has been said that organisms which cause dangerous post-operative wound infections are derived from soil and road dirt, and that therefore such material should be kept out of theatres. The author suggests that if it should be found that these organisms are present in outdoor air it may prove desirable, when designing ventilating and air-conditioning plant for operating theatres, to provide for the recirculation of air.

Thomas Bedford

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOOD POISONING

BESSLER, C. & PROJA, M. Tossinfezioni alimentari in Italia nel triennio 1955–1957. [**Food Poisoning in Italy during the Three-Year Period 1955–57**] *Ann. d. San. Pubblica.* Rome. 1959, Sept.–Oct., v. 20, No. 5, 955–78. [16 refs.] English summary (8 lines).

The authors have already published a report on bacterial food poisoning as it occurred in the previous 3-year period [this *Bulletin*, 1957, v. 32, 266] and the present paper is comparable. These food infections are not notifiable in Italy. The authors report for each year the incidence and mortality, the geographical—north, centre and south—and seasonal distribution and the various classes of food incriminated. Fresh meat and offal, cream pastry and fish pastes were the vehicles most frequently encountered. The third quarter of the year showed the highest incidence, followed by the second quarter. With the introduction of school meals and other welfare feeding, the first 2 quarters of 1956 showed many outbreaks due to reconstituted milk powder.

Public health authorities have since circulated appropriate advice for the guidance of those who have to manage this programme of welfare feeding. The health and habits of those entrusted with the handling of this dried milk require special attention. Carriers should be sought by periodic medical examination, and excluded from this work when found. This staff should be trained to understand the hazards involved and to follow correct practices. The reconstitued product provides a favourable medium for the growth of bacteria, including those which give enterotoxin, and there should be as short an interval as possible between reconstitution and consumption. The most scrupulous cleanliness of equipment is essential. Every batch of dried milk powder must be submitted to bacteriological and chemical examinations before it is passed for use.

Food poisoning is not notifiable in Italy but 246 incidents, involving 5,183 persons with 15 deaths, are known to have occurred in 1955. In 52% of the outbreaks the cause remained unidentified. Of the remainder, 55% are attributed to a staphylococcus, 36·5% to salmonellae and 8·5%—10 outbreaks—to other bacteria. Of these last, 3 outbreaks are attributed to *Shigella sonnei* and 1 to *Shigella flexneri*. England and Wales for the same year recorded 8,961 incidents, the cause of 3,447 [38·4%] of which remained unidentified; 5,269 [58·7%] incidents were attributed to salmonellae [this *Bulletin*, 1957, v. 32, 357]. In the U.S.A., in 1955, salmonellae were considered responsible for 16—namely 15·5% of all incidents.

[Tables accompanying this paper show *Salm. paratyphi B*, as the cause of some of the incidents: a clinical picture of food poisoning, as distinct from an enteric illness, from *Salm. paratyphi B* figured prominently in the 1955 outbreaks north of Nottingham.]

The data for this paper were derived from various sources, mainly public health laboratories and health authorities.

J. Cauchi

DEWBERRY, E. B., **Food Poisoning: Food-Borne Infection and Intoxication. Nature, History and Causation. Measures for Prevention and Control.**

This book was reviewed on p. 626.

WADE, C. H. T. **Food Poisoning from Cold Chicken.** *Med. Officer.* 1959, Dec. 24, v. 102, No. 26, 334–5.

38 of 41 members of a coach party and 88 of 115 persons at a wedding reception suffered diarrhoea and abdominal pain 6 to 12 hours after meals of cold chicken. Heat-resistant *Clostridium welchii* were isolated from 5 faeces samples from the coach party, from 9 of

the wedding guests and also from chicken remaining from the wedding meal, which had been simmered for 4 hours on the previous day and allowed to cool slowly overnight in the liquor.

The source of the *Cl. welchii* is discussed.

[Chicken was described as a vehicle of *Cl. welchii* food poisoning by McCLUNG, this *Bulletin*, 1946, v. 21, 326; see also McKILLOP, *ibid*, 1959, v. 34, 918.]

Betty C. Hobbs

CAMERON, A. D. C. S. **A Localised Outbreak of Paratyphoid B Fever (Phage-Type Taunton).** *Med. Officer.* 1959, Dec. 24, v. 102, No. 26, 330–34.

Of 22 persons ill with paratyphoid fever in Central London, *Salm. paratyphi B* phage type Taunton was isolated from 21. 18 of these patients lived in one metropolitan borough. 4 were seriously ill, the remainder were mildly affected. The average length of stay in hospital was 43 days because it was difficult to obtain bacteriological clearance even with repeated courses of chloramphenicol, tetracycline and other antibiotics. Women and children were mainly infected.

Except in 4 cases it was possible to relate the infection either directly or by secondary spread within a household to consumption of confectionery sold by 2 local and associated shops. At one of these shops the night baker, responsible for cream cakes and other confectionery, was found to be excreting *Salm. paratyphi B* phage type Taunton without symptoms.

3 cases only, probably secondary, occurred after this baker ceased duty for treatment, which was successful, and the baking was discontinued while thorough cleansing and redecoration took place.

Imported frozen whole egg in use at the time of the investigation was negative for salmonellae although flaked albumin showed Salm. Bareilly, Salm. Amager and Salm. Tennessee.

The infection of the night baker by imported frozen whole egg and the subsequent contamination of cream cakes and other confectionery is suggested. The pasteurization of egg products is strongly recommended.

[Although the batch numbers of the frozen whole egg relevant to this investigation were not available, it was found later that *Salm. paratyphi B* phage type Taunton was present in the frozen whole egg imported in October 1958, and available in Spring of 1959.]

Betty C. Hobbs

SHVEDOV, L. M. **Neutralization of Toxin formed in the Alimentary Tract in Experimental Toxicoinfection with *Clostridium botulinum* Type A by Parenteral Administration of Antiserum.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 1, 95–100. [Translated from Russian.]

Experimental work on rabbits, mice and guineapigs infected orally with small multiples of the MLD of a culture of *Cl. botulinum* type A.98 showed clearly that the administration of antiserum to the upper alimentary tract was more efficacious than intramuscular injection. This was effected in the rabbit by an operative procedure which fixed the duodenum on the base of a wound made to expose the abdominal contents, the antisera being injected through the duodenal wall. In the smaller animal diluted antiserum was introduced by sound to the stomach.

The conclusions are drawn (a) that continued production of toxin in the intestine is an important factor in disease, and (b) that in man the oral route of serum administration should be adopted, as has already been done in a small number of cases by Minervin, with good results. The dose should be 50 million units in 300–400 ml. of boiled water, introduced by duodenal sound, or even by deep enema. *J. W. McLeod*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

LIU, Yuan-Kuao. **A New Method of Micro-Culture for Fungi.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 2, 191–4, 3 figs.

A slide culture chamber for fungi is described by this author which permits microscopical study of these organisms during growth.

The slide, which is thick, and able to stand on its edge, is made of porcelain and has a square window cut out in a central depression. This window can be converted into a culture chamber by applying a sealed coverslip on either side. A funnel-shaped canal through the roof of the chamber communicates with the exterior and can be plugged with cotton wool or covered with a metal lid. Agar medium can be introduced through this canal into the chamber. After inoculation this culture slide is placed on moist blotting paper in a box and the box is put in the incubator.

The author suggests different ways of arranging the agar medium in this chamber for different purposes.

C. J. La Touche

FINDLAY, G. H. **Ringworm (Tinea) Infections in the Transvaal.** *Med. Proc.* Johannesburg. 1959, Oct. 3, v. 5, No. 20, 429–33, 1 fig.

125 cases of ringworm seen in Pretoria between 1955 and 1958 are reviewed. 63 cases were tinea capitis due mainly to *Microsporum canis* infection (57 cases); the remainder were due to *Trichophyton violaceum* (4) and *M. gypseum*. The pre-school child was mainly affected with a maximum incidence at the age of 5 years.

Tinea corporis (12 cases) was usually caused by *M. canis*, acquired from dogs or cats. Tinea cruris (14 cases) and tinea pedis (35 cases) were usually negative for fungus or culture though *T. mentagrophytes* was isolated once from the groin and occasionally from the foot. This species was also found in the only case of tinea barbae.

Peter Abbott

EVOLCEANU, R. & LAZAR, Maria. Le problème de l'existence et de la mise en évidence des ferments kératinolytiques chez les dermatophytes. [**The Existence and Recognition of Keratinolytic Ferments in Dermatophytes**] *Mycopathologia.* The Hague. 1960, Mar. 31, v. 12, No. 3, 216–22. [11 refs.]

MCCUISTION, C. H., Jr., LAWLIS, Marjorie G. & GONZALEZ, B. B. **Toxicological Studies and Effectiveness of Griseofulvin in Dermatomycosis.** *J. Amer. Med. Ass.* 1959, Dec. 19, v. 171, No. 16, 2174–80, 4 figs.

This is a clinical and toxicological study of 32 patients in a mental hospital who were treated with griseofulvin. Although most of the patients were of prepubertal age (6–13 years) some of them were much older.

3 of these patients had involvement of the nails. The remainder had tinea capitis or mixed tinea capitis and tinea corporis. Tinea capitis cases included 12 patients infected by *Trichophyton tonsurans*, 1 by *T. schönleini*, 1 by *T. violaceum*, 4 by *T. rubrum*, 5 by *Microsporum audouini*, and 2 by *M. canis*. There was one case of infection of the feet due to *Candida parakrusei*.

In the case of children suffering from tinea capitis griseofulvin was administered orally in daily doses of 0·5 gm. to 1·0 gm. (occasionally 2 gm.) and withheld at the end of the 6th week. The patients' heads were then shaved, and again at the end of 14 weeks from the date on which therapy had been instituted. All patients with tinea capitis recovered except one who refused to have her hair cut.

Treatment of the patients with nail infection was being continued but all 3 had shown a favourable response to the drug. The patient with *C. parakrusei* infection of the feet did not respond at all.

Blood counts and urinalysis were carried out before and at weekly intervals during treatment and the blood counts were repeated 6 weeks after the treatment had been discontinued. A number of other laboratory tests were performed.

The only significant side-effect of treatment was a "right shift in the peripheral blood cell count which began after drug was used." There was no significant change in the white cell count although it rose significantly "6 weeks after therapy was discontinued."

C. J. La Touche

SASLAW, S., CARLISLE, H. N. & SPARKS, Joann. [**Experimental Histoplasmosis in Monkeys.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 342–4. [15 refs.]

"Severe disease was produced in monkeys by yeast phase *H. capsulatum* administered intravenously and intratracheally. Monkeys inoculated intranasally exhibited a more mild disease process. No significant clinical signs of illness were seen in monkeys inoculated by the gastric route."

CAMPBELL, P. J. & HESELTINE, W. W. **An Apparent Growth Stimulant for *Candida albicans* released from Tetracycline-Treated Bacterial Flora.** *J. Hygiene.* 1960, Mar., v. 58, No. 1, 95–7.

"The results reported in this preliminary communication suggests that tetracycline acts on the bacterial flora of the human throat and the mouse intestine in such a way as to make available an unidentified 'growth factor' for *C. albicans*. Multiplication of yeasts as a result of tetracycline therapy would therefore seem to be due to such a factor rather than ecological changes.

"Increase in the development of mycelial elements in the presence of filtrates from tetracycline-treated throat and faecal cultures was an incidental observation, but it is interesting to speculate on the possibility that this induced increase in the development of pseudomycelium might reflect a change from relatively saprophytic growth towards a form with greater pathogenic potential."

PAPAZIAN, C. E. & KOCH, R. **Monilial Granuloma with Hypothyroidism. Report of a Case treated with Amphotericin B.** *New England J. of Med.* 1960, Jan. 7, v. 262, No. 1, 16–18, 4 figs. [12 refs.]

This is a clinical report of a case of monilial granuloma associated with hypothyroidism in a 14-year-old girl.

A history of chronic *Candida* infection dating from infancy preceded the onset of the granulomatous lesions. At infancy she had thrush, and at 10 months a "yeast-type blood infection". At the age of 4 years her fingernails and scalp became involved. In due course the cutaneous surfaces of the perianal and perivaginal areas became involved and also the corners of the mouth and eyelids. At 8 years the patient developed anaemia and at 10 years the gastro-intestinal tract became involved. At this time the lesions in the scalp became more prominent.

On examination the anterior portion of the scalp and forehead were covered with "thick scaly plaques and yellowish-brown horny lesions on an erythematous base." The nails and tips of the fingers were also involved.

Laboratory investigations revealed *Candida* in culture from the scalp and from the finger-nails.

Biopsy preparations from the scalp showed, besides various tissue reactions, "scattered, elongated, slightly nodular, occasionally branching hyphae."

Topical therapy consisted in the application of a lotion "composed of copper sulphate (5 gm.) zinc sulphate (15 gm.) in distilled water *ad* 240 ml. and ointment containing 5% salicylic acid and 8% resorcinol. Nystatin ointment, 100,000 units per gm. and 2·5% hydrocortisone ointment were also applied as well as amphotericin B ointment. Response was, however, slow and it was finally decided to administer amphotericin B in a dosage of "0·5 mg. per kilogram of body weight intravenously per day." Altogether, the patient received 31 doses totalling 363 mgm. of amphotericin B intravenously. She experienced various side reactions throughout the course of treatment. Marked improvement resulted from this treatment by the 71st day. For the hypothyroidism, "thyroid 0·12 to 0·2 gm. (2 to 3 grains), was given daily."

The patient was discharged with instructions to continue to apply amphotericin ointment to the scalp. On examination 6 months later "no evidence of recrudescence of the granulation on the scalp or forehead" was observed. *C. J. La Touche*

FELISATI, D., BASTIANINI, L. & DE MITRI, T. **Antibiotics and *Candida albicans* given by Endobronchial Route.** *Antibiotics & Chemotherapy.* New York. 1959, Dec., v. 9, No. 12, 744–51, 4 figs. [13 refs.]

Rabbits were given an intratracheal injection of 5 x 10^7 *Candida albicans* spores, with or without an added antibiotic: the antibiotics were also given alone. Animals were killed and the lungs examined 12 hours or 7 days later. Antibiotics alone caused some haemorrhagic changes. *Candida albicans* alone produced small inflammatory nodules near the hilum. When penicillin (10,000 units), streptomycin (10 mgm.) or chloramphenicol (10 mgm.) was added, the changes were the same. When the addition was 10 mgm. of tetracycline or chlor- or oxytetracycline, extensive inflammatory lesions going on to suppuration were produced throughout the lungs. *L. P. Garrod*

BRADLEY, S. G. & FARBER, P. J. **Interactions among *p*H, Buffer, and Nystatin in *Candida stellatoidea*.** *Antibiotics & Chemotherapy.* New York. 1960, Mar., v. 10, No. 3, 174–9, 3 figs.

PIMSTONE, B. L. & SAUNDERS, S. J. **Aspects of Cryptococcosis.** *South African J. Lab. & Clin. Med.* 1959, Sept., v. 5, No. 3, 156–69, 1 fig. [33 refs.]

The clinical features and associated laboratory findings of 14 cases of cryptococcosis occurring in Cape Town over a period of 13 years are reviewed, the cases being divided into 4 categories according to the type of infection presented by the patient. These were: "Cryptococcosis associated with Chronic Disease"; "Pulmonary Cryptococcosis"; "Osseous and Cutaneous Cryptococcosis"; and "Cryptococcosis of the Central Nervous System."

The chronic disease with which cryptococcosis was associated was, in one case (a child) chronic nephritis and in the other (an elderly woman) diabetes mellitus.

5 patients presented with pulmonary cryptococcosis. In 2 of these the lesion was localized, and in one which could be followed up recovery followed after excision of the lesion.

A patient suffering from chronic rheumatoid arthritis presented with acute arthritis of the right elbow in which there was bone destruction. Subsequently the patient presented with a cutaneous lesion also over the right shoulder.

Patients suffering from cryptococcosis of the central nervous system could be classified into several subgroups, namely: "Cases suggestive of a subacute meningitis"; "Cases simulating a space-occupying lesion" and cases presenting with "terminal central nervous system involvement in widespread dissemination."

In the authors' opinion amphotericin B is a more promising drug in the treatment of this infection than others hitherto used for this purpose. Oral administration was not very effective on account of poor absorption of the drug by the gastro-intestinal tract; it may be tried in cases where the central nervous system is not yet involved. Intramuscular dosage at 0·125 mgm. per kgm. 3 times a week has been reported as being satisfactory in certain cases. Intrathecal administration of this drug in doses of 0·5—1 mgm. in 5 ml. of water has also been recommended in cases where the central nervous system is involved. *C. J. La Touche*

MUMENTHALER, M. Meningoencephalitis durch *Cryptococcus neoformans.* [**Meningoencephalitis caused by *Cryptococcus neoformans***] *Schweiz. med. Woch.* 1960, Apr. 2, v. 90, No. 14, 386–91, 9 figs. [57 refs.]

The English summary appended to the paper is as follows:—

"The author presents a personal case of meningoencephalitis caused by Cryptococcus neoformans (Torula histolytica)—in a 69 year old housewife—which was diagnosed anatomo-pathologically. It is the fourth such case to be observed in Switzerland. On the basis of the literature, the clinical, diagnostic, differential diagnostic, anatomo-pathologic, mycologic and the therapeutic aspects of an infection by Cryptococcus neoformans are discussed."

FELDMAN, R. **Cryptococcosis (Torulosis) of the Central Nervous System Treated with Amphotericin B during Pregnancy.** *Southern Med. J.* 1959, Nov., v. 52, No. 11, 1415–17. [14 refs.]

The author describes a case of cryptococcosis in a pregnant woman aged 19 who was treated with amphotericin B and who eventually gave birth to a normal child.

The patient became ill in March 1958, at which time she was pregnant. Her symptoms included: nausea, vomiting and headache, and among other signs of disturbance of the central nervous system she had ataxia, palsy of the 6th nerve on the left side and bilateral papilloedema. *Cryptococcus neoformans* was recovered from the cerebrospinal fluid.

Treatment with amphotericin B was instituted on July 28th, 1958. This drug was administered in a dosage of 25 mgm. in 5% dextrose and water intravenously for 6 hours. In addition, she was given tetracycline by mouth and by injection. Treatment with amphotericin B was discontinued on August 13, but was resumed 2 days later at a higher dosage (50 mgm. daily). No organisms were found in the cerebrospinal fluid at this time or subsequently. On September 12, the patient received a dose of 75 mgm. of amphotericin B to which she reacted with "a shaking chill followed by emesis". A litre of whole blood was thereupon administered and she showed marked improvement. However, the clinical course continued to be intermittent until the patient was delivered of a 6 lb. normal male infant on December 23.

In mid-January 1959, the patient returned to hospital after a "grand mal" seizure. Amphotericin B in the dosage of 50 mgm. 3 times a week was again administered as well as anticonvulsants, whereupon the patient again showed clinical improvement and was discharged. *C. J. La Touche*

TOIGO, A. **Pulmonary Aspergillosis.** *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 392–6, 6 figs. [20 refs.]

"A case of pulmonary aspergillosis with several unusual features is described. The disease disseminated rapidly throughout both lungs while the patient felt and appeared well. There were multiple abscesses in both lungs. A sudden, lethal pulmonary hemorrhage occurred, but the source of this could not be demonstrated at autopsy."

BAYLET, J., CAMAIN, R. & SEGRETAIN, G. Identification des agents des maduromycoses du Sénégal et de la Mauritanie. Description d'une espèce nouvelle. [**Identification of the Aetiological Agents of Maduromycosis in Senegal and Mauritania. Description of a New Species**] *Bull. Soc. Path. Exot.* 1959, July–Aug., v. 52, No. 4, 448–77, 18 figs. on 4 pls. [27 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 753.]

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

HEAF, F. **Tuberculosis in Adolescence.** *Practitioner.* 1960, Mar., v. 184, No. 1101, 322–30, 1 fig. [15 refs.]

Approximately 1 in every 5 notifications of tuberculosis in England and Wales in 1958 was in the 15-24 years age-group. This calls for greater efforts to prevent the development of progressive disease and to eliminate the risk of exposure of young persons to infection.

Tuberculosis in adolescence arises from the exacerbation of a dormant lesion due to primary infection in childhood or to primary exogenous infection in adolescence producing progressive disease.

Evidence of the importance of primary infection during adolescence is shown by the natural reactor rate rising with age coupled with a comparatively high incidence of active disease soon after tuberculin conversion.

It is also possible that infection in childhood is responsible for some of the lesions in the 15-24 age-group, and there is evidence that the degree of sensitivity following recent conversion is related to the risk of developing active post-primary disease in the future.

The prevention of tuberculosis in adolescents must be based on the following measures:

1. BCG vaccination of all non-reactor adolescents.
2. Intensive search for all infectors in the community.
3. The discovery of all recent infections by mass tuberculin surveys in children followed by treatment or chemoprophylaxis.

Tuberculosis in adolescence can be present for a considerable period and produce only vague symptoms. All reactors who feel unwell over a period should therefore be X-rayed. In addition to mass radiography surveys routine X-ray examination of all young persons attending clinics and hospitals is recommended.

When beds are available all adolescents with tuberculosis should be treated initially in hospital, and only exceptionally should they be given domiciliary treatment. In underdeveloped countries mass methods of prevention by vaccination from infancy onwards, mass radiography,

widespread domiciliary treatment and efforts to raise the standard of living are the only ways to reduce the number of infectors. *H. G. Calwell*

ARBLASTER, P. G., CROSS, K. W. & SPRINGETT, V. H. **Respiratory Tuberculosis in the Birmingham Region.** *Brit. J. Preventive & Social Med.* 1959, Oct., v. 13, No. 4, 194–203, 6 figs.

This article sets out to review the changes which have taken place in tuberculosis over the past 10 years in the Birmingham region. It starts with a series of graphs showing the fall in the mortality rate, males and females being separated; there was a dramatic fall in all the age-groups in the males, except in those of over 65; the younger the age-group the greater the fall. The same tendencies are evident in the females, except that in the older age-groups the fall has been very considerable as opposed to that of the males. The notification rate, both male and female, showed little change until 1954, when a slow decline began, accelerating in 1957; a marked difference between the 65 plus group and the others in males is not apparent.

The sources of new cases in the years 1955–57 are analysed, and show that cases referred by general practitioners totalled 54%, notified by hospitals 19%, the mass miniature radiographic service excluding general practitioner referrals—7%, contact services 10%, and other sources 10%. The mass radiography service accounted for one quarter of the newly notified cases. As regards the stage of disease in newly diagnosed cases, information is not available centrally for the region as a whole, but for the county of Warwickshire, population 550,000 for 1951-57, details are available. The number of males in 1956 at each stage was as high as in 1951, although the number of extensive cases during 1957 was much lower. The number of minimal cases in women in 1956 was much greater than in 1951. A considerable increase has taken place in the number of cases on the clinic register since 1951, and the 1957 figure exceeds that for 1951 by more than 50%. This is undoubtedly due to the improved survival of tuberculosis patients arising from new methods of treatment.

As regards the number of patients on the register known to have a positive sputum during the preceding 6 months, there has been a steady fall with a dramatic decrease since 1952. The fate of these patients has not been studied on a regional basis, but in the Wolverhampton area, population 150,000, 14% of infectious patients remain so classified 2 years later and almost two-thirds of these are drug-resistant.

In the 13 areas with schemes operating BCG vaccination the percentage of children for whom skin testing and vaccination is accepted varies between 41% and 93%.

Scrutiny of chest clinic attendances showed that between 1949 and 1953 the number of new patients seen annually more than doubled, but since 1953 has fluctuated somewhat below the 1953 peak, and the pattern for re-attendance is rather similar.

Facilities for chest X-ray examination at the request of general practitioners are now available throughout the region.

The number of patients attending for mass radiography examination rose dramatically from about 100,000 in 1949 to just under 400,000 in 1954, after which the figure settled at just over 350,000. The yield of cases per 1,000 examined rose to a peak of 5·7 per 1,000 in 1952, with a subsequent decline to 3·1 per 1,000 in 1957.

The number of refills given at the Birmingham Chest Clinic in 1958 was about 4% of those given in 1953.

The number of beds rose to a peak in 1952, and remained about the same until 1958, when it was planned to reduce the allocated beds by 631 within 3 years. In 1952 the effective bed occupation was about 100%, and by 1957 there was an average of 557 staffed unoccupied beds each day. This resulted in only 44 patients awaiting admission at the end of 1958.

The number of patients admitted for surgical treatment reached a peak of 1,336 in 1954, but dropped to 647 in 1957. The proportion of resections to thoracoplasties has steadily risen during the last few years.

F. H. Young

WATERS, M. H. **Two Outbreaks of Tuberculosis in Service Establishments.** *Med. Officer.* 1960, Apr. 1, v. 103, No. 14, 193–5, 1 fig.

The outbreaks of tuberculosis described here both occurred in Scotland in 1956–57.

In the first an airman aged 20 became ill with symptoms suggestive of pneumonia. He was found to have extensive bilateral pulmonary tuberculosis with cavitation and positive sputum.

The other 21 men who shared the same sleeping hut were tested with tuberculin by Heaf's method. The number of reactors is not stated. 5 of the non-reactors were found to be reactors when retested about 7 weeks later. X-ray examination of these 5 has not shown evidence of tuberculosis to date.

Another man showed early infiltration in one lung. Resection was done, and there was pathological and bacteriological evidence of tuberculosis. This man and 3 of those who underwent tuberculin conversion occupied beds close to the first patient. There was a family history of tuberculosis in both cases of pulmonary tuberculosis.

The other outbreak occurred in a military barracks occupied by some 600 soldiers. A soldier aged 18 years became ill and was found to have a pleural effusion with a fibrotic pulmonary lesion. Tubercle bacilli were not found in his sputum. Guineapig inoculation failed; there is no mention of culture.

In the ensuing 5½ months 2 men were found with open pulmonary tuberculosis and 1 with active tuberculosis of a joint. A mass radiography survey yielded 2 cases of active and 1 of inactive tuberculosis.

3 of the men found to have active pulmonary tuberculosis had served in Egypt recently in an area where tuberculosis is prevalent.

297 soldiers were tuberculin tested, of whom 64·6% reacted. The reactor rate rose with age (50–75%).

The author advises X-ray examination of military personnel every 6 months, tuberculin testing and BCG vaccination in units with large numbers of young men, and thorough examination by a chest physician of all men with symptoms suggestive of chest disease.

H. G. Calwell

MOURIER, P. Resultatet af tuberkuloseundersögelserne i forsvaret 1946–58. [**The Result of the Tuberculosis Investigations in the Fighting Forces 1946–58**] *Ugeskr. f. Laeger.* 1960, Mar. 17, v. 122, No. 11, 375–82, 5 figs.

During the period under review there have been changes in the strengths of the tuberculins used for Mantoux testing. There have also been changes in the frequency of negative tuberculin reactions. Thus during the first 4 years about 33% of the recruits called up for service were negative. Negative reactions have diminished to such an extent that by 1958 only 10% were negative. This change is traced to the BCG vaccinations carried out among schoolchildren who are thus rendered positive before being called up. It is expected that this 10% will be still further reduced. But with BCG vaccination still being voluntary, a small body of objectors to it can be counted on to prevent complete unanimity.

After discounting minor X-ray changes in the chest such as deformity of the ribs, cervical rib, calcified primary foci, situs inversus, etc., there remained 5,063 cases composed of 2 almost equal groups, 2,282 reflecting tuberculosis, 2,781 non-tuberculous diseases. For these groups combined, this gives a pathological find of 0·71% for the whole period under review or about 2 persons for every 300 examined. During this period there has been a great fall in the incidence of tuberculosis in recruits, but since 1953 the tuberculosis rate among them has been fairly constant. As for the non-tuberculous diseases, 92% of them were represented by one or other of the 4 following ailments: pneumonia, pulmonary infiltration, adenitis thoracis and lymphogranuloma benigna. The corresponding rate for civilians is only 46·9%. In other words, more than half the ailments of the respiratory tract of civilians do not belong to any of the 4 above-mentioned diseases. *Claude Lillingston*

BTESH, S. **Tuberculosis in Israel. Mortality and Morbidity Trends in the Various Ethnic Groups.** *Israel Med. J.* 1958, Nov.–Dec., v. 17, Nos. 11/12, 245–52, 7 figs.

During the period 1948-51 687,000 immigrants entered the State of Israel. Only a few were examined on entry in 1948 but in the following years nearly one-half were examined, and it was found that the incidence of active tuberculosis was about 6 per 1,000 compared with a rate of 1 in the settled population of the country in 1947.

The highest incidence was in immigrants from Turkey, 9·3 per 1,000. The rates in immigrants from eastern European countries were 5·1 to 4·2, from North Africa 2·3, from Iraq 2·1, Iran 1·9, Yemen 0·8, and from other Asian countries 1·4.

Analysis of the behaviour of the disease in the various racial groups was not possible for the years 1948-51 owing to lack of information but it was possible to analyse the data for the years after 1952.

Eastern European Jews were found to have a high infection rate and high resistance with the exception of new immigrants whose resistance was low. A great many of these had been in concentration camps where the unfavourable environment had caused both greater infectivity and a lowering of resistance.

Yemenite Jews and Israeli Arabs had a low infection rate and a low resistance. The Yemenite Jews also had been living in extreme poverty before entering Israel.

North African, Asian and native Israeli Jews had a low infection rate and high resistance. *H. G. Calwell*

ANDERSEN, S. & GESER, A. **The Distribution of Tuberculous Infection among Households in African Communities.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 1/2, 39–60, 7 figs.

The data analysed here were collected in 8 different African territories and 1 large city from 1955–58, *viz.* Basutoland, Bechuanaland, Swaziland, British Somaliland, Tanganyika Territory, Uganda, Ghana, Nigeria and Ibadan.

Groups of the population randomly selected to form a representative sample were surveyed. In all 34,200 persons were examined belonging to 70 population groups and living in 6,680 separate households.

All were tested intradermally with 5 TU of PPD and sputum was collected for examination from all persons judged to be over 12 years of age. X-ray examination could not be done systematically.

The presence of tuberculous infection was indicated by finding a tuberculin reaction of 13 mm. or over in children up to the age of 14 years; the range was 9–29·2% positive.

It was found that there was an excess of households with many or all children infected as well as of households with no children infected. Infection was not evenly distributed. There was evidence that it was accumulated in certain households.

The bacteriological examination available was such as to detect only the most extensive infections. In all 12 persons were found to be expectorating tubercle bacilli (a range of 0·3–2·4% of those examined), and only 3 of the 6,680 households had more than a single infectious person. Analysis of the distribution of these open cases did not reveal accumulation of infection in certain households but there was a slight tendency for open cases to occur in households where the reactor rate was higher than average.

The conclusion reached is that in regions comparable to those surveyed tuberculosis control measures should be applied widely to the whole population and not only to households considered to be specially exposed.

H. G. Calwell

SANKALÉ, M., PLESSIS, J., DUCLOUX, M. & GENTILINI, M. L'endémie tuberculeuse dans la région de Gao (République Soudanaise). [**Endemic Tuberculosis in Gao, Republic of Sudan**] *Bull. Soc. Path. Exot.* 1959, Sept.–Oct., v. 52, No. 5, 587–91.

An X-ray apparatus was installed in Gao for the first time in 1957 and within 6 months 137 new cases of pulmonary tuberculosis were discovered in addition to the 25 already known and there were also 57 of extra-pulmonary tuberculosis; the total population was 6,200 and the disease rate for pulmonary tuberculosis alone was

therefore over 25 per 1,000, which is extremely high. 60% of the patients with pulmonary tuberculosis had cavities and 75% were sputum positive on direct examination.

The authors make a special point of tuberculosis in men who have returned from working in Ghana, and these represented half the cases in the local Songhai tribe, who are cultivators. There were fewer cases in nomad Africans (but it is not clear what proportion of the total population was made up of nomads).

A treatment centre is to be built, and the authors advise that a small occupational unit should be incorporated. Treatment is based on rest and chemotherapy, and prophylaxis with BCG is advised. Particular emphasis is placed on the importance of supervision of men who have worked in Ghana.

Charles Wilcocks

FRIMODT-MØLLER, J. **A Community-Wide Tuberculosis Study in a South Indian Rural Population, 1950–1955.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 1/2, 61–170, 25 figs. [33 refs.]

This paper would make profitable reading for any person engaged in public health work in an underdeveloped area as it gives details of the organization of a tuberculosis survey under primitive conditions.

In 1948-49 a tuberculosis survey by mass radiography and tuberculin testing was begun in the town of Madanapalle in South India (population 14,000 in 1948 and 20,000 in 1955). In 1950 about 200 scattered villages were included making a total population for study of about 60,000.

The rural inhabitants are mostly farmers who are ordinarily well fed but in times of drought the poorest section may suffer from scarcity of food. Plague, cholera and malaria are endemic. Worm infection is common.

During the period 39,496 persons were tested with tuberculin and 25,092 retested at least once; 31,889 were X-rayed once and 18,711 more than once. By the end of the survey 85% of all available inhabitants had received at least 1 tuberculin test or been X-rayed or both. Movement of population and illiteracy made the keeping of records very difficult.

The Mantoux test with Danish PPD was used (1, 5, 10 and 100 TU). Reactions, as defined, were positive at 5, 10 and 20 years respectively as follows: to 1 TU, 9, 12 and 28%; to 10 TU 27, 35 and 72%; to 100 TU, 58, 80 and 98%; to 5 TU, 22, 28 and 54%. It was thought that most of the low-grade sensitivity was due to unknown acid-fast organisms. Retesting showed that there was a considerable degree of variation in sensitivity which may have been due to genuine fluctuation or to variations in the technique of testing. These variations made it difficult to estimate the infection rate; it may be 2–4% annually.

The X-ray surveys yielded a discovery rate of active pulmonary tuberculosis of 5·4 per 1,000 males and 2·8 per 1,000 females. The prevalence in children was very low, being 0·5 below 10 years.

The annual incidence of fresh cases of active disease was 0·46 and 0·41 per 1,000 males and females respectively. Rates at 20-29 years were 0·54 and 0·59 respectively. Fresh cases of active disease were seen only in persons with initial reactions of 10 mm. or more to 5 TU.

The results of a trial of BCG vaccination were disappointing in that it was not possible to demonstrate any protective effect. As post-vaccinal tuberculin sensitivity was found to be at a very low level it was considered possible that the vaccine had lost its potency owing to damage by heat or sunlight. Other factors that might have interfered with the effect of the vaccine are mentioned.

The average annual death rate for tuberculosis was 49 per 100,000. The rate before the start of the investigation was 200 or more. The rate fell steadily throughout the period to 21, which must be ascribed to the detection of the disease in its earlier stages and the wide use of antibiotics. Despite the great fall in mortality no significant change in the prevalence of tuberculosis during the period was found. *H. G. Calwell*

TAO, Jung-Chin & CHANG, Cheng-Chi. **Pulmonary Tuberculosis among the Aboriginal Population in Taiwan.** *J. Formosan Med. Ass.* 1959, June 28, v. 58, No. 6, 307–32, 5 figs. (1 coloured). [17 refs.]

The aboriginal population of Taiwan (Formosa) numbered 145,867 in 1958. The area they inhabit is 45% of the whole area of the island but they represent only 2% of the total population.

105 villages were covered by the tuberculosis survey reported here, and the inhabitants of these villages numbered 70,000 among whom 15,123 were under 5 years of age and 38,204 were over 15. Of the children under 5, 13,970 were tuberculin tested (Mantoux, 5 TU of PPD), and the results were read in 12,732 (84·2%).

The coverage rate of the tuberculin survey ranged from 99 to 30%. Many of the children had been vaccinated with BCG previously, and 10% of all those tested had vaccination scars. Groups with more than 10% showing vaccination scar were excluded from the analysis of the survey.

The total reactor rate among children without vaccination scars was 9·2% (3·2 to 20·0%). Total rates were 1% at 0–1 year and 18·7% at 4–5 years. Reactions fell into 2 groups, *viz.* 0–10 mm. and 16–17 mm. It was considered that large reactions were due to tuberculous infection and the small reactions occurred in the uninfected.

34,781 persons over 15 years of age in the aboriginal villages were X-rayed. Pulmonary tuberculosis was suspected in 1,307 (3·8%). Incidence rates ranged from 7·5% to 1·7%. The disease was minimal in 55%, moderate without cavity in 23%, moderate with cavity in 6% and far advanced in 15%. There was pleural effusion in 1%. The disease was more advanced in patients from the north than from the south. "On the whole, tuberculosis is very prevalent among the aboriginal population of Taiwan." *H. G. Calwell*

NYBOE, J. **The Efficacy of the Tuberculin Test. An Analysis based on Results from 33 Countries.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 1/2, 5–37, 9 figs. [15 refs.]

This study included some 190,000 persons tested in 33 countries in Africa, America, Asia and Europe in 1950-58 by WHO teams. The population groups tested were not selected at random but this is not believed by the author to impair the validity of his conclusions.

The Mantoux test was used with 5 TU of PPD but owing to the adsorption of the tuberculin on to the glass of the vials this dose was later estimated to have been only about 2 TU. Non-reactors to the 1st test were tested with 100 TU in some groups.

The number tested varied from 450 in Mexico to 48,000 in the Sudan; in most countries it ranged from 3,000 to 10,000. About 44% were schoolchildren and the rest were all ages.

Reactions were measured (mm. of induration), and the sensitivity pattern indicated that in some countries there was a clear division between positive and negative reactions at 10 mm. so that with this criterion the proportion misclassified would be small. In other countries however the pattern was not bipartite so that it was not possible to distinguish sharply between positive and negative.

Clarity of distinction between 2 kinds of reaction varied considerably from country to country but the observations made suggested that climatic conditions rather than geographical latitude determine the pattern of sensitivity and that there exist in tropical surroundings certain factors that impair the efficacy of the tuberculin test as an indicator of tuberculous infection.

The tuberculin test will have to be improved for use in tropical countries. *H. G. Calwell*

JOHNSTON, W. W., SALTZMAN, H. A., BUFKIN, J. H. & SMITH, D. T. **The Tuberculin Test and the Diagnosis of Clinical Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 189–95. [21 refs.]

The use of the tuberculin test as an aid to differential diagnosis is more complex than its use in mass surveys of apparently healthy persons.

The finding of FURCOLOW *et al.* [this *Bulletin*, 1942, v. 17, 697] that 99·6% of 468 patients with proved tuberculosis had reactions of 5 mm. or more to 5 TU or less of PPD was found to be contrary to the clinical experience of the present authors who therefore carried out a retrospective study on patients with tuberculosis in 2 American hospitals.

In a trial in which PPD was used 81 patients admitted consecutively and later proved to have tuberculosis gave reactor rates of 84% to 1 TU and 93·9% to 5 TU. 5 patients (6·1%) failed to react to 5 TU and 1 to 100 TU. Details of reactions and types of disease are given.

In the other trial OT was used. The results obtained in 120 patients with proved tuberculosis are given. Only 69% reacted to 10 TU or less, and 85% reacted to 100 TU. Among the 120 patients 26 were diagnosed without sputum culture. When these were excluded from the analysis as possibly containing a high preponderance of atypical acid-fast infections the reactor rates to 10 and 100 TU respectively were only 66% and 84%.

Clinical and experimental evidence is produced that when chemical irritation occurs the reactions begin before the 6th hour after injection and are readily differentiated from true allergic responses. False positive reactions to 1,000 TU of OT were not seen in experimental animals. Tuberculin sensitivity may be due to infection from an atypical acid-fast organism or a true tubercle bacillus.

It can be accepted that high tuberculin sensitivity is accompanied by greater risk of developing clinical disease. Relative immunity is assured by low-grade allergy, except, for the most part, in cases of overwhelming infection. [See also this *Bulletin*, 1960, v. 35, 364.] *H. G. Calwell*

KATZ, S., DUVALL, R. C., RYAN, T. J., O'CONNOR, T. F., MARILLY, R. J. & PERRY, R. B. **Intermediate-Strength Purified Protein Derivative. Its Diagnostic Significance in Active Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 196–9, 1 fig.

This is an evaluation of the Mantoux test in the diagnosis of active tuberculosis.

416 patients with proved tuberculosis were tested with 5 TU of PPD. The disease was classified as far advanced in 78%, moderately advanced in 20% and minimal in 2%.

386 patients (92·8%) reacted with induration of at least 5 mm. at 48-72 hours. 30 patients (7·2%) did not react to the initial test but did so when given the same dose of tuberculin after an [unspecified] interval.

All but 1 of the 7 patients who failed to react to either test had obvious causes of anergy: 3 were dying, 1 was in a very toxic state with gangrene of a limb, 1 had miliary disease and was being treated with corticosteroids, 1 had coexisting sarcoidosis, and the remaining patient displayed no apparent cause for failure to react.

The importance of repeating the test in a patient with an initially negative or doubtful reaction, when it would be expected to be positive, is stressed.

The interval between tests may be a week or longer. If a patient was toxic or suspected of having transient tissue anergy retesting was often deferred until clinical improvement took place.

The authors concluded that regardless of the clinical or X-ray findings, if the Mantoux test with 5 TU of PPD is negative on 2 occasions and no obvious cause for anergy exists, the patient is unlikely to have tuberculosis. *H. G. Calwell*

HALL, Zaida M., ZORAB, P. A. & JEFFERSON, K. E. **Chemotherapy for Radiographically Stable Tuberculous Lesions.** *Tubercle.* 1960, Feb., v. 41, No. 1, 47–50.

This study was planned in order to determine whether any advantage could be obtained by giving a year's prophylactic antituberculous drugs to those who had apparently radiologically stable lesions. 80 patients, 5 men, and 29 women between the ages of 29 and 79 who

attend regularly the Paddington and Kensington Chest Clinic, London, were included in the study. All had pulmonary shadows which were assumed to be tuberculous in origin, and considered not to have changed for at least 3 years. For one reason or another these 80 had to be whittled down to 55; 27 of these were treated by approximately 10·5–12 gm. of calcium benzoyl PAS, and 230–300 mgm. of isoniazid daily. 18 continued to take the drugs for 9–12 months, 4 for 5–8 months, and 3 for 1–4 months. 2 patients took too small a dose in error. The reason for ceasing to take the drugs was nearly always dyspepsia. 28 patients were not treated and merely observed.

Of the 27 patients, 3 improved radiologically, and none deteriorated; these 3 had taken the drugs for 12, 10, and 8 months respectively. Of the 28 untreated patients, none improved radiologically, and 1 patient deteriorated, and in the untreated group 2 have subsequently deteriorated.

The small scale of the trial does not allow the answer as to whether prophylactic treatment of this kind should be carried out, but the authors consider that the investigation of a larger series might be worth while.

F. H. Young

BATTEN, J., TURNER-WARWICK, Margaret, HOYLE, C. & NICHOLSON, H. **Prolonged Drug Treatment for Pulmonary Tuberculosis.** *Lancet.* 1960, Feb. 20, 409–12.

This paper is an amplification and continuation of that in the *Lancet* by HOYLE, *et al.* [this *Bulletin*, 1956, v. 31, 382]. The original records of these were subsequently lost in a fire, but this study is believed to include the vast majority of them, and also records of some patients under the care of 2 of the authors.

The study deals with 193 patients, who all received antituberculous drugs for at least 9 months. 171 of these patients have been observed for 2 years, and 134 for 3 years after completing drug treatment. 75 were treated surgically and by other methods as well as with drugs; of the other 118 patients drug therapy was the only definitive treatment. The 2 groups were similar as regards the presence of cavitation, but a rather higher proportion of patients treated with drugs alone had extensive disease. 152 patients were receiving antituberculous drugs for the first time. 41 had had previous treatment for short periods, regarded as inadequate by present standards, and 35 of these were in the group of 118 patients treated by drugs alone.

The final results of treatment were judged by the ability of patients to resume and continue their normal lives. Relapse was recognized by radiographic extension of disease, by the appearance of cavitation, or by return of a positive sputum. Drug regimes varied from patient to patient and over the years of the study, but all patients were treated with combinations of 2 or 3 drugs accepted as effective by the Medical Research Council standards.

With 1 exception all patients were admitted to hospital and rested in bed for the first 3 to 6 months. Tubercle bacilli were isolated from the sputum of 140 of the 193 patients. Only 1 had a persistently positive sputum after completing treatment, although in 5 others bacilli continued to appear in the sputum for a year; in these the sputum became negative within the next 2 years while the same drug regime was continued. 116 of the 193 patients had cavities, which were closed by drugs alone in 53 instances; in the earlier years of the study many patients were treated surgically within a year after drug treatment was started, and for this reason the influence of drug therapy on cavity closure cannot be fully assessed. In 30 out of 60 patients treated by drugs alone the cavities closed within 6 months, and in a further 19 after 6 months to 3 years. 11 patients in this group were left with persisting cavities, but in only 1 did the sputum remain positive. 14 patients of the whole series had persisting cavities at the time drugs were stopped. 9 of these are alive with open cavities and a negative sputum, but 6 had a positive sputum at the end of treatment or subsequently; 3 have died of tuberculosis and 1 of respiratory failure. [The character of the persistent cavities is not mentioned.]

Of the 193 patients 23 (12%) relapsed from the beginning of treatment up to 4 years after drugs were stopped. 6 of these patients relapsed while receiving chemotherapy, but 17 (8%) relapsed after drug treatment was completed. Of 118 patients treated with drugs alone, 3 relapsed during treatment and 15 (13%) relapsed subsequently. 8 patients relapsed who had had over 18 months' continuous drug treatment. 19 of the 23 patients who relapsed are now well, with their disease stabilized. 5 of them were treated surgically and 2 had an artificial pneumothorax. 6 received further therapy for about 2 years, while the remaining 6 were not given any further treatment but have remained well. 1 is receiving further chemotherapy. The remaining 3 of the 23 who relapsed have died—2 from non-tuberculous causes and 1 from advanced tuberculosis.

11 patients died during the 8 years of observation—5 from tuberculosis, 3 from respiratory failure, and 3 from unrelated causes.

Of the patients followed for 3 years after completion of drug treatment, 123 of the 134 have survived. 6 have open cavities but are well with a negative sputum, 17 have relapsed at some time within the 3 years, and 6 have severe breathlessness with bronchitis and are respiratory cripples. 116 are well and have resumed work.

Persisting cavitation in association with a positive sputum is a very serious condition in that 4 out of 6 such patients died.

Spread of the disease to a new site or the finding of a positive sputum in the absence of radiological change was rare.

A number of tables are appended which bring out the points made in the text very clearly. *F. H.Young*

AUERSBACH, K., BARTMANN, K., KAUFFMANN, G. W., KREBS, A., SCHÜTZ, I. & STEINBRÜCK, P. Die frühe Erkennung der Risikofälle bei konservativ-chemischer Behandlung der kavernösen Lungentuberkulose. [**Assessment of Prognosis in Pulmonary Tuberculosis with Cavitation by Response to Chemotherapy**] *Wiener med. Woch.* 1960, Apr. 2, v. 110, No. 13, 293–6, 3 figs.

The object of this investigation was to obtain criteria on which to base an assessment of the probability of

a successful outcome of treatment. The authors are aware that the prognosis must be based on other factors also in addition to those presented.

They studied some 212 patients in 2 hospitals. All had been examined by tomography, their tubercle bacilli were initially sensitive to the drugs used, and any previous treatment with drugs had been at least 1 year before the present treatment.

The course prescribed was a combination of isoniazid (at least 5 mgm./kgm. daily) with streptomycin (at least twice weekly 1·0 gm.) or PAS (at least 9 gm. daily orally or intravenously) or both. Its duration was at least 6 months before discharge or surgical operation.

There were 121 patients with thick-walled cavities; favourable progress was seen in 105 at the end of 3 months of whom only 4 had not maintained their improvement at the end of 6 months. Only 3 of 76 failed to maintain improvement at the end of 9 months.

There were 44 patients with a pneumonic form of the disease in whom the cavity wall could not be clearly defined apart from the surrounding infiltration. 39 showed favourable progress at the end of 3 months, 34 of 41 at the end of 6 months and 31 of 34 at the end of 9 months.

There were 47 patients with thin-walled cavities, of whom all showed improvement at the end of 3 months, 46 maintained their improvement at the end of 6 months and 28 of 29 at the end of 9 months.

A scheme of prognosis based largely on bacteriological findings, X-ray appearances and sedimentation rates is given in tabular form. Thick-walled cavities require most intensive treatment. In the pneumonic form of the disease the most important criterion for prognosis is the blood sedimentation rate. Thin-walled cavities cause least concern. *H. G. Calwell*

MONEY, G. L. **Spastic Paraplegia complicating Isoniazid Therapy.** *West African Med. J.* 1960, Feb., v. 9 (n.s.), No. 1, 3–6. [10 refs.]

After mentioning the variety of nervous disturbances which are recognized as a complication of the use of isoniazid, especially in high doses, the author describes 3 patients who developed spastic paraplegia complicating isoniazid therapy. These were seen at Ibadan during the session 1957-58.

Case 1. This occurred in a 28-year-old Yoruba schoolmaster. He had been treated for 3 months with the 3 recognized drugs in conventional doses, and subsequently treated himself with isoniazid 300 mgm. daily from illegal sources. He had ingested isoniazid for almost 2 years when he was first seen. For 9 months before admission he had developed pains and paraesthesiae, and 2 months before admission he was unable to walk. Physical examination revealed spastic paraplegia but normal higher functions and cranial nerves. Isoniazid was withdrawn and he was treated with Becosym injections daily for 30 days and a balanced hospital diet. [Becosym contains various vitamins of the B group.] After 14 weeks' treatment he could walk and run though the tendon reflexes in the legs were slightly exaggerated. Later he developed acute riboflavin deficiency symptoms; these yielded to riboflavin 30 mgm. daily after 14 days.

Case 2. This 27-year-old Yoruba policeman wa treated with isoniazid and PAS (including 300 mgm isoniazid daily) for 18 months. During the last 2 month of treatment he suffered from painful dysaesthesiae i the hands and feet. When admitted to hospital he wa found to have a spastic paraplegia. The isoniazid wa discontinued and he was treated with ordinary hospita diet supplemented with pyridoxine 50 mgm. daily, an 6 tablets of yeast. At the end of 8 months he was ab to walk quite well, but there was still mild spasticity slightly exaggerated reflexes and extensor planta response.

Case 3. A 14-year-old Yoruba schoolboy was treate with isoniazid 300 mgm. daily and PAS 12 gm. daily At the end of 6 months he had made excellent progres and thinking he could treat himself he stopped attendin and took isoniazid alone 600 mgm. daily. He the developed a spastic paraplegia. Isoniazid was not with drawn but he was treated with Becosym tablets. Afte 2 weeks' treatment there was some improvement, h defaulted from out-patients and was not seen for months. His gait had improved gradually over a perio of 6 months and when reviewed he could walk normally He was perfectly fit and was doing a full day's work a a petrol station.

The author thinks that the recurrence of severe nervou disturbance among patients receiving isoniazid in rela tively low dosage—2–4 mgm. per kgm. body weight—i due to the coexistence in these patients of deficienc disease which isoniazid unmasks. *F. H. Young*

PETERS, J. H., with the technical assistance of R. LARSE & A. TABRI. **Studies on the Metabolism of Iso niazid. I. Development and Application of Fluorometric Procedure for measuring Isoniazi in Blood Plasma.** *Amer. Rev. Respiratory Di* 1960, Apr., v. 81, No. 4, 485–97, 6 figs. [29 refs.]

PRESCOTT, B., KAUFFMANN, Gladys & STONE, H. **Means of increasing the Tolerated Dose o Isoniazid-Streptomycin Mixtures in Mice. II Certain Vitamins.** *Antibiotics & Chemotherapy* New York. 1960, Mar., v. 10, No. 3, 163–8.

"With the goal of reducing toxic manifestations i mice, due to isoniazid-streptomycin mixtures, 14 vitamin have been used as adjuvants with various mixtures o the two therapeutic agents in two strains of mice. A mixture of 5 mg. streptomycin and 2 mg. isoniazid individually nontoxic by subcutaneous administration permitted only one third of the animals of either strai to survive. With vitamins as adjuvants in such mixture, however, each of 11 in white mice and eac of four in DBA mice permitted 90 to 100% survival With double these amounts of the therapeutic agents calcium pantothenate and nicotinic acid were 100 an 90% effective in white mice, and 73 and 42% in DBA mice. Nicotinic acid (25 mg.) permitted DBA mice t survive 20 daily administrations of a mixture of 2 mg isoniazid and 5 mg. streptomycin."

PEPYS, J., MITCHISON, D. A. & KINSLEY, B. J. **The Prevalence of Bacterial Resistance to Isoniazid and to PAS in Patients with Acute Pulmonary Tuberculosis presenting for Treatment in East Africa.** *Tubercle.* 1960, Feb., v. 41, No. 1, 32–6.

A number of therapeutic trials have been undertaken in East Africa from 1958 to 1959. The method and place of examination of the bacilli for resistance is detailed. In the Uganda trial of 1953–55 no initial resistance was found to isoniazid (56 patients), PAS (26 patients), or streptomycin. In the sulphone trial of 1956 initially isoniazid-resistant strains were found in 7·9% of 140 patients, and PAS-resistant strains in 2·9% of 69 patients.

In the thiacetazone pilot trial of 1957, 7·5% of 40 patients were found to have bacilli resistant to isoniazid. PAS sensitivity was not examined in this trial. In the isoniazid trial of isoniazid alone in low and high dosage, and isoniazid plus PAS (1957) isoniazid resistance was found in 12·6% of cultures from 151 patients tested in Britain, and in 16% of cultures from the whole group of 162 patients tested in the East African laboratory. PAS resistance was reported in 10·7% of 75 initial cultures.

In the thiacetazone/diphenylthiourea trial of 1958–59, isoniazid resistance was found in 9·9% of the initial cultures from 172 patients, and PAS resistance in 4·1%.

Although the patients selected were supposed not to have had previous treatment with the antituberculous drugs it is certain that an appreciable number had taken them in some shape or form. The authors were not able to determine whether this high degree of resistance was due to irregular ingestion of the drugs or whether infection had been obtained from patients who had drugs already resistant. *F. H. Young*

THOMAS, H. E. **A Retrospective Study of Cases of Pulmonary Tuberculosis developing Drug Resistance.** *Tubercle.* 1960, Feb., v. 41, No. 1, 37–46. [23 refs.]

This paper tries to find out why drug resistance appears in some patients and not in others. During 1956–57 about 30,000 cultures were done in a small laboratory in Birmingham. From resulting positive cultures 2,500 sensitivity tests were done, and according to a definition laid down in the paper on minimal inhibitory concentrations 182 were found to be resistant to isoniazid, PAS, or streptomycin singly or in combination. From these, 61 patients were selected, 44 males and 17 females, in whom it was reasonably certain that more than 1 drug had been given throughout. A control group was obtained by matching each resistant case with the patient nearest to the same age and of the same sex on the tuberculosis register whose disease confirmed bacteriologically did not develop resistant bacilli. The groups were not matched for radiological factors, acuteness of diseases, etc., although the resistant group had considerably more disease than the non-resistant.

As regards the type of disease, cavitation was present in 56 of the resistant group, and 30 of the non-resistant group, and 3 of the resistant group cavitated later. 6 of the resistant group had homogeneous round foci, as against 1 in the random group. The proportion of patients having only 1 cavity was twice as great in the random series as in the resistant series. As regards the size of the cavities, 21% of the resistant group had cavitation below the equivalent of 4 cm. in diameter, as against 87% of the random group. Thus it was found that the following factors were more common in the diagnostic radiograph in those developing bacterial resistance than in the random group; an extent of disease greater than the equivalent of 2 zones, and cavitation especially if it is multiple, or if the largest has a diameter greater than 4 cm. across.

Comparison between the place where treatment was started and the type of treatment given suggested strongly that in a high proportion of the resistant group the chemotherapy had been inadequate, either because of the use of intermittent streptomycin or more frequently because it was strongly suspected that the patients were not taking their PAS regularly.

The author suggests that all patients having any of the radiological factors which have been found to be associated with resistance should have their chemotherapy completely in hospital for at least 6 months if emergence of drug resistance is to be avoided. *F. H. Young*

WEISS, W., EISENBERG, G. M. & FLIPPIN, H. F. **Kanamycin and Sulfisoxazole in the Treatment of Pulmonary Tuberculosis. A Clinical Note.** *Antibiotic Med.* New York. 1959, Dec., v. 6, No. 12, 731–3.

Kanamycin has been reported to have considerable anti-tuberculous activity *in vitro* and in experimental animals with little toxicity. Sulfisoxazole has been reported to have anti-tuberculous activity *in vitro*. The authors have confirmed the *in vitro* activity of both these drugs.

They examined 23 strains of tubercle bacilli which were found to have been susceptible to kanamycin in a concentration of 10 μgm./ml. and in 21 of the strains susceptible to Sulfisoxazole in concentrations of 2 to 15 mgm. per 100 ml. *in vitro*. 10 patients, all of whom had advanced pulmonary tuberculosis, were treated with kanamycin, of whom 5 received also Sulfisoxazole in addition; an additional patient had to have isoniazid as well so is not included. The scheme was to treat patients for 6 months; the therapy was discontinued after 1 to 5 months in 9 patients, because of therapeutic failure in 3, toxicity in 4, and both therapeutic failure and toxicity in 2. In the 4 patients who had toxic disease, defervescence did not occur during the first 4 weeks of treatment, although the fever gradually disappeared later. Permanent sputum conversion did not occur in any patients. At the end of therapy all the patients on kanamycin alone were excreting organisms resistant to it, at a level of 10 μgm./ml. Of those treated with both drugs, only 1 showed organisms resistant to 10 μgm./ml. of kanamycin. Very little radiological improvement occurred during the period in which the drugs were being exhibited.

From the toxic point of view urinary analysis showed more or less constant cylindruria in all but one of the

patients. 4 patients developed albuminuria at 2 to 4 months of therapy.

Eighth cranial nerve damage was apparent clinically in 4 patients at 1 to 5 months treatment. In 1 there was vestibular disturbance, and auditory nerve damage in 3.

All patients, except 1, had 1 gm. of kanamycin intramuscularly each day; 1 patient received 1·5 gm. daily, and complete deafness appeared after 2 months of therapy. Hence kanamycin as used was found to have a low-grade therapeutic effect and a high degree of toxicity for the eighth cranial nerve and the kidneys. Sulfisoxazole may delay the emergence of resistance to kanamycin. The authors suggest that it may be worth while to investigate the ability of Sulfisoxazole to delay the emergence of resistance to other antituberculous agents. *F. H. Young*

KAKIMOTO, S., NISHIE, J. & YAMAMOTO, K. **Studies on the Antitubercular Compounds (XVIII) Synthesis of a Vinylog of Isonicotinic Acid Hydrazide.** *Japanese J. Tuberculosis.* 1959, Dec., v. 7, Nos. 2/4, 76–80, 1 fig.

HILTZ, J. E., SCHAFFNER, V. D. & KLOSS, G. A. **Pneumonectomy for Tuberculosis: an Evaluation of 124 Cases.** *Canadian Med. Ass. J.* 1960, Feb. 27, v. 82, No. 9, 457–63. [14 refs.]

This paper describes 124 cases in whom pneumonectomy was performed for tuberculosis and analyses the complications met with and the results obtained. 20 of the operations were performed before 3 standard drugs were available. The authors suggest that the fistula syndrome in its variations is responsible for a high proportion of the complications. A table is given showing the complications related to the side of operation and the previous operative procedures. Of the 124 pneumonectomy operations, 57 (46%) developed one or more of the complications. The 57 persons had a total of 135 complications either singly or in combination. Apart from the early operative mortality the significant complications may be classified as contralateral spread of disease, and the fistula syndrome. Most of the spreads cleared rapidly and may have been non-tuberculous or possibly tuberculous lesions implanted at sites unsuitable for their maintenance owing to antimicrobial therapy. Speaking generally, the age-group 50–59, especially males, suffered most greatly from complications. Complications developed more frequently on the right side. There did not seem to be any significant relationship between the likelihood of developing complications and a history of previous surgery in the same lung. However, when 3 procedures had been undertaken previously upon the same person, the complication rate was significantly higher than when 1 or 2 had been carried out. This suggests only that the underlying disease was of a more chronic and persistent nature and more prone to complications. Complications were found to be more frequent when the sputum was positive, and in the presence of cavitation. These suggested the presence of tubercle bacilli in the bronchial stump.

59% of the cases had either destroyed lung or demonstrable cavitation, and this group accounted for 74% of all cases with complications. The presence of cavitation, especially if the cavity was large was a considerable factor, but not the only one in the development of empyema. 28 of the 31 instances of empyema were accompanied by demonstrable bronchopleural fistulae.

Unfortunately no worth-while figures were available regarding the pre-operative drug resistance for tubercle bacilli. Of the 108 persons who had had their operation for 2 years or longer, 51 were greatly improved, and 2 improved with negative sputum. Of the 84 who had their operations 5 or more years ago, 52 (62%) were classified as much improved. Of the 35 persons in the 10-year group, only 6 are known to be alive, 21 having died of tuberculosis, and 8 of non-tuberculous causes. There were 11 deaths in the first 60 day post-operative period giving a rate of 9%. A comparative table of mortality and post-operative complications quoted by various authors is given. *F. H. Young*

KASS, I., MIYAMOTO, T., DENST, J., WITTENSTEIN, G. I. RUSSELL, W. F., Jr., MIDDLEBROOK, G. & DRESSLER, S. H. **The Residual Lesion in Pulmonary Tuberculosis requiring Surgery. A Review of 100 Sputum-Negative Patients Consecutively Operated on.** *New England J. of Med.* 1960, Feb. 18, v. 262, No. 7, 315–20. [13 refs.]

One of the most debatable problems in those countries where adequate treatment for all kinds of tuberculosis is available is whether patients who have become sputum negative as a result of antimicrobial therapy should be submitted to surgery. This paper consists of a report on 100 consecutive patients with sputum negative for tuberculosis who were submitted to surgery between January 1956 and January 1958 in Denver, Colorado. 56 of these patients had been sputum-positive on admission to hospital, the remaining were negative and stayed negative before surgery. The antimicrobial treatment given was fully adequate in all cases. Where the organisms were found to be resistant either to streptomycin or to isoniazid or both, PAS and isoniazid were the drugs used. Where there was no resistance, streptomycin, 1–2 gm. per day for at least 3 months, and isoniazid for at least 18 months was given; the dosage of each drug being determined by serum assay studies [this *Bulletin*, 1960, v. 35, 135]. PAS was used in this group not primarily for its antimicrobiol activity but rather to raise the serum level of microbiologically active isoniazid [*ibid.*, 1957, v. 32, 615].

The 100 patients were divided into 4 groups. Group 1 consisted of 34 patients who had previous antituberculosis treatment, and on admission had sputa that were negative for tubercle bacilli on smear and culture; Group 2, 17 patients who had prior therapy and whose sputa contained organisms resistant to either streptomycin or isoniazid or both; Group 3, 39 patients who were excreting typical tubercle bacilli susceptible to both isoniazid and streptomycin; Group 4, 10 patients who had received no previous anti-tuberculous therapy, but had negative sputum upon admission.

All patients when submitted to operation had had conversion of the sputum and absence of further marked changes in the X-ray films of the chest. The patients with sputum positive on admission were consistently negative on smear and culture for an average of 20 weeks before surgery. Patients with sputum negative on admission were operated on about 23 weeks after admission.

The indication for surgery fell into 8 groups. Immediately after resection histological sections were prepared including staining by the Ziehl-Neelsen method if smears had not revealed tubercle bacilli previously. The principal lesion in 34 of the specimens was an open cavity, and in 52 it was a closed necrotic lesion. The remaining 14 specimens were not cultured.

Of the 10 open-cavity cases in Group 1, 3 were completely negative but only 2 had a positive culture. In Group 2, 5 were completely negative, and 1 had a positive culture. Of the 16 cases in Group 3, 5 were completely negative, and none had a positive culture. Of the 2 cases in Group 4, 1 was negative and none had a positive culture.

In the closed necrotic nodule group the results were as follows: Group 1, 24 cases. 3, including 2 patients excreting anonymous yellow bacilli were completely negative and none had a positive culture. Of the 7 cases in Group 2, none were completely negative and 3, including 2 excreting anonymous yellow bacilli, had positive culture. In the 25 cases in Group 3, 3 were completely negative and 2 had a positive culture. Of the 6 cases in Group 4, 1 was completely negative, and none had positive cultures. Thus 89% of the closed necrotic lesions contained tubercle bacilli obtainable by some method, as opposed to 63% of the open cavities. Thus in persistently negative sputa patients the nodular lesions appear to be less amenable to the effects of chemotherapy than the open cavity. Details are also given of 260 patients admitted to the hospital between December 1953 and December 1956 and who were not submitted to surgery as they had a negative sputum. Of these only 1 had a positive sputum as far as was known in 1957. In the present series no patients had positive sputa at the time of re-examination but this statement depends on the patients' reports.

The authors conclude that in the type of patients dealt with in this report the following remain indications for surgery: (1) Round lesions of undetermined aetiology because of the possibility of cancer. (2) Symptomatic tuberculous bronchiectatic lesions especially the left-upper-lobe syndrome. (3) Excretion of drug-resistant organisms before conversion; this includes anonymous mycobacteria. (4) Where the serial sputa show a precipitous decline in bacterial content early in the course of chemotherapy. Here the change is often attributable to bronchocavitary blockade rather than direct chemotherapeutic effect. (5) Ethnic predisposition to progressive tuberculosis and sociological factors precluding adequate therapy or follow-up study. Resection is not indicated where the residual lesions are in sputum-negative patients who at the time of admission to hospital had negative bacilli or were excreting populations of tubercle bacilli susceptible to isoniazid and streptomycin; neither is it advised for those whose previous clinical history or current course revealed a prompt bacteriological conversion of the sputum, who can continue to tolerate adequate and sustained therapy with streptomycin, isoniazid or PAS, if the isoniazid blood level is low, and who are likely to carry out the treatment advised.

[This is an excellent paper which deserves to be read *in extenso*. One only regrets that 100 was the total number of patients who were available for analysis.]

F. H. Young

ERDÖS, Z. & GEFFERTH, K. **The Clinical Course of Acute Miliary Tuberculosis in Children Vaccinated with BCG.** *Acta Med.* Budapest. 1960, v. 15, Nos. 1/4, 117–28, 12 figs.

"Four cases of miliary tuberculosis observed in children vaccinated with BCG have been reported. Of the 4 patients, 3 showed a typical miliary pattern, while the fourth displayed submiliary patchy nodules of varying size.

"Recovery was considerably quicker than in non-vaccinated children. Apart from the remarkably favourable and immediate response to treatment, regression of the X-ray manifestations was unusually rapid. Disappearance of the foci took not more than a month, in one case not even two weeks. Such a rate of improvement has never been experienced in non-vaccinated patients.

"Accordingly, BCG vaccination not only mitigates the clinical course of miliary tuberculosis but also enhances disappearance of the morphological changes."

VENEREAL DISEASES

LARSEN, A. A. & CUNNINGHAM, W. J. **Venereal Disease Facilitation in Vancouver, British Columbia.** *Canadian J. Pub. Health.* 1960, Feb., v. 51, No. 2, 49–56.

A facilitator is a person who assists someone who may well be suffering from venereal disease to meet a healthy person. In order to find out to what extent facilitation existed in Vancouver, 1,005 male patients suffering from acute gonorrhoea were questioned. As regards places of meetings, 32·5% named beer parlours, 18·6% cafés, 22·2% streets, 4·5% private homes, 4·4% cabarets, 3·1% dance halls, 2·7% hotels and 11·1% "other"; places of exposure were hotels 46·5%, rooming houses 19·4%, private homes 13·8%, autos 12·3% and other 5·9%. Methods of introduction were "pick-up" 53·3%, acquaintance 27·3%, solicitation 8·4%, mutual acquaintance 8·3%, procuring 1·5%, not stated

9%. In the large majority of cases the patient sought the girl and knew nothing about her but knew where to take her. A certain limited number of hotels were frequently named, in these the desk clerk made no attempt to find out why the couple required a room; in two-thirds of beer parlours the management allowed men to enter the part reserved for females—against the regulations.

Medical officers of health have no power to deal with facilitators but legislation against them exists, though its enforcement is evaded by many of them. Brothels and procurers do not appear to be common in Vancouver.

T. E. Osmond

SAMANT, M. S., RAO, S. S. & MODY, B. G. **A Comparative Study of Kahn, Meinicke and VDRL Flocculation Tests for Serodiagnosis of Syphilis.** *J. of J. J. Group Hosps. & Grant Med. College.* Bombay. 1960, Jan., v. 5, No. 1, 25–31. [25 refs.]

In order to assess the relative value of these 3 reactions, these authors tested 4,602 sera in parallel; 42% were reactive with VDRL, 38% with Meinicke (MR) and 36·8% with Kahn. Of 1,930 sera reactive with VDRL, 204 (10·6%) were non-reactive with the other 2 tests; of 2,647 sera non-reactive with VDRL, 19 (0·72%) were reactive with MR and 12 (0·45%) with Kahn. Of 1,312 known syphilitic sera, VDRL was positive in 1,064, MR in 992, and Kahn in 961; of 2,492 doubtful syphilitic sera the positive reactions were, 800, 679 and 682 respectively; of 798 non-syphilitic sera the respective numbers of positive reactions were 58, 60 and 50. MR gave the highest number of false positive reactions and Kahn the lowest. Full details are set out in 6 tables. It is concluded that the VDRL is the best test as giving the most positive reactions in syphilis and roughly the same number of false reactions as the other two.

T. E. Osmond

SANDERS, R. W., PIPER, D. R., HOOK, W. A. & MUSCHEL, L. H. **Nonspecific Immobilization in the *Treponema pallidum* Immobilization (TPI) Test.** *Amer. J. Clin. Path.* 1960, Feb., v. 33, No. 2, 135–7.

This phenomenon may occur and "no valid test" may be reported if a serum contains antibiotics or certain other drugs, or if there are physiological abnormalities, or if toxic substances develop in the serum during transit.

To overcome this difficulty, these authors separated the euglobulin fraction and submitted this to the TPI test. The separation was carried out by taking 1 volume of serum (1 ml.) and adding 9 volumes of 0·0027 N HCl. The mixture was placed in an ice bath for 30 minutes, then centrifuged at 2°C. for 20 minutes at 2,000 g. The supernatant was removed and the precipitate dissolved in 0·5 ml. of saline. The euglobulin solution was heated at 56°C. for 30 minutes and then tested in the ordinary way, being made up to half the amount of the original serum. 148 such specimens were tested and 117 (79%) gave satisfactory results, 9 non-toxic sera were tested whole in parallel with their euglobulin fractions and results agreed closely. *T. E. Osmond*

EVANG, K. & MELLBYE, F. Behandling av kjönnssyk dommer. [**Treatment of Venereal Diseases** *Tidsskr. f.d. Norske. Laegeforening.* 1960, Apr. 1 v. 80, No. 8, 412–13.

The Norwegian Government undertakes to defray th cost of drugs for treatment of venereal disease provide they conform to certain requirements. They must, fo example, figure on the list of drugs for venereal disease issued from time to time by the Health Directory as guide to the medical profession. A check on thei prescription is effected by the rule that requisitions fo payment are passed on by chemists to the Healt Directory, which has discovered that many concer drugs absent from the Directory's list. Reason for such deviations not having been given, the Director has issued the present memorandum, which outline briefly the latest and most authoritative views on th choice of drugs and their dosage. [It should be note that Dr. Evang is at the head of the Directory.]

Penicillin, notably in the form of PAM-penicillin, i the drug to be preferred, no penicillin-resistant strain o the treponeme of syphilis having yet been observed. Onl when there is a record of complications following th administration of penicillin should it be dispensed with and replaced by some other antibiotic. The administra tion of penicillin by mouth is to be discouraged fo various reasons. The dosage by injection should b 1·2 million units in 2 days (600,000 on each day) earl in the incubation period (the first week after infection) Later in the incubation period, 2·4 millions should b given in 4 days (600,000 on each day); for primary an secondary syphilis, 6 millions in 10 days (600,000 o each day). The same holds for latent syphilis. Fo "benign" tertiary syphilis the dosage is 6 millions, fo cardiovascular syphilis, 6–9 millions, for neuro-syphilis 10–20 millions, for syphilis congenita precox, 1·3 millions and syphilis congenita tarda, 6 millions. If neither penicillin nor any other antibiotic can be given, the tediou and troublesome combined neosalvarsan-bismuth cours may be used, for in the long run it appears to be a effective as pencillin.

For gonorrhoea, when it is not complicated, an injec tion of 600,000 units of penicillin should suffice. Her again penicillin should be given by injection rather tha by mouth, but if the latter cannot be avoided, a table containing 250,000 units should be given 4 times dail for 2 days. Complications call for the extension of thi period to 6 to 8 days. Penicillin-resistant strains of th gonococcus having been observed, it may be necessar to switch off to some other antibiotic. Streptomycin 0·5 gm. given by intramuscular injection daily for 3 t 4 days will cure gonorrhoea in most cases.

Claude Lillingston

HOO, C. C. *Trichomonas vaginalis* **Infestation. A Study of the Morbidity in One Thousand Women** *Proc. Alumni Ass., Malaya.* 1959, Dec., v. 12, No 4, 182–9. [24 refs.]

This author in Singapore examined 1,000 marrie women of various races for the presence of *Trichomona vaginalis* (TV) by direct smear, using a low powe objective; the organisms were clearly detected mainl

by the activity of the flagella (C) and undulating membrane. Lubrication of the speculum used did not appear to affect the organisms, pregnant and non-pregnant women were almost equally affected (at about 14·2%) and the *p*H of the vagina was usually 5 or higher. Leucorrhoea and vaginitis appeared to favour infection but cervicitis and cervical erosions without leucorrhoea or vaginitis less so. The incidence of infection was much the same in all age-groups from 15 to 45, after which it tended to rise.

Almost all the infected subjects were symptomless [which is not the experience in Great Britain], the male is almost the only known reliable source for infecting women, and this accounts for many reinfections after apparent cure; the female urethra is said to be an important source of auto-reinfection. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and Other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

REBHAN, A. W. & EDWARDS, H. E. **Staphylococcal Pneumonia: a Review of 329 Cases.** *Canadian Med. Ass. J.* 1960, Mar. 5, v. 82, No. 10, 513–17, 4 figs.

A series of 329 cases of staphylococcal pneumonia in children treated at the Hospital for Sick Children, Toronto, between 1950 and 1958 showed that the disease was increasing as was the percentage of staphylococci resistant to penicillin, streptomycin and tetracyclines. Not more than 14% were resistant to erythromycin nor more than 11% to chloramphenicol: none were shown resistant to bacitracin or novobiocin. Selection of the appropriate antibiotic or combination of antibiotics reduced mortality: a combination of chloramphenicol and erythromycin proved very effective, but when that failed bacitracin or novobiocin was used with success. Empyema was a frequent complication and usually required drainage. Of the total, 32% of patients had some hospital contact before illness, but, of fatal cases, 74% had such contact: 83% of fatal cases were in children under 1 year old. *A. B. Christie*

YKELENSTAM, P. A. Stafylokokken-diarree op een chirurgische afdeling. [**Staphylococcus Diarrhoea in a Surgical Ward**] *Nederl. Tijdschr. v. Geneesk.* 1960, Apr. 9, v. 104, No. 15, 720–26. [20 refs.]

The English summary appended to the paper is as follows:—

"Twenty cases of diarrhoea in a surgical ward are presented. A description is given of a form of diarrhoea which occurs in patients shortly after an operation, and is caused by resistant staphylococci. This complication, which may also arise without surgical intervention, is mostly fatal, unless immediate action is taken. The chances of recovery are better if the infection is diagnosed and treated before the onset of diarrhoea.

"A drastic curtailment of the use of antibiotics and isolation of patients under antibiotic treatment may be of value in preventing this dreaded complication."

BRANDT, L. & SWAHN, B. **Subacute Bacterial Endocarditis due to Coagulase-Negative** *Staphylococcus albus.* *Acta Med. Scandinavica.* 1960, Feb. 17, v. 166, No. 2, 125–32.

This is an important article which draws attention to the increasing incidence of subacute bacterial endocarditis due to coagulase-negative *Staphylococcus albus.* When this organism is found in a blood culture it is usually dismissed as a contaminant, but if symptoms suggestive of bacterial endocarditis persist, the finding may be significant and further blood cultures should be done.

5 cases are fully described; the organism was isolated from the blood 4, 2, 4, 11, and 4 times respectively. The clinical picture was usually similar to that of endocarditis lenta due to *Streptococcus viridans,* but the course was very variable. The prognosis is rather poor, although the organism is usually sensitive to all the commonly used antibiotics. Septicaemia due to *Staph. albus* is nearly always associated with endocarditis, in this respect resembling septicaemia due to *Strep. viridans* and contrasting with that due to *Staph. aureus* where the cardiovascular system is involved only in 25% of cases. Among the 5 cases described, 3 followed the operation of digital commissurotomy, and 2 of these were fatal.

As a rule the patients have predisposing factors in their history, usually rheumatic heart disease. The increase in the number of operations upon the heart and great vessels during the last decade has resulted in an increase of post-operative staphylococcal endocarditis. Of all cases of bacterial endocarditis 75–85% are due to *Strep. viridans* and 5–15% to enterococci; staphylococci are responsible for about 5%, of which 1% has been estimated to be due to *Staph. albus* [SMITH *et al., Arch. Intern. Med.,* 1958, v. 102, 375]. The latter figure is probably increasing. Treatment with large doses of penicillin may be recommended. Benzyl penicillin 6–10 million units daily for at least 4 weeks was used successfully in 3 of the 5 cases described. *H. Stanley Banks*

COPE, S., SANDERSON, G., ST. HILL, C. A. & CHAMBERLAIN, E. N. **Prophylactic Use of Oral Penicillin in Rheumatic Fever, Chorea, and Carditis.** *Brit. Med. J.* 1960, Mar. 26, 913–17.

In 3 successive years 40 patients at St. Joseph's Children's Heart Hospital, Rainhill, were observed for evidence of streptococcal activity or rheumatic infection: in the first year, no specific prophylactic was given, in the second year penicillin V tablets 60 mgm. were given twice daily, and in the third year penicillin G tablets 200,000 units twice daily. The penicillin regimes did not prevent rheumatic activity. In the penicillin V period there were 4 cases of rheumatic fever compared with 5 in the first period. The penicillin G period showed better results but not significantly better. Penicillin blood levels were certainly theoretically adequate. There was evidence of rise in anti-streptolysin O (ASO) level on several occasions but only once in 3 years was a group A beta haemolytic streptococcus isolated on a throat swab.

The authors suggest that such rises in ASO may mean that the streptococcus is present in some inaccessible site, provoking antibody response but, in the absence of a third factor, not producing rheumatism. The authors hope that larger doses of penicillin may produce better results. *A. B. Christie*

LIM, W. N. & WILSON, May G. **Comparison of the Recurrence Rate of Rheumatic Carditis among Children receiving Penicillin by Mouth Prophylactically or on Indication. A Six-Year Study.** *New England J. of Med.* 1960, Feb. 18, v. 262, No. 7, 321–5. [16 refs.]

The authors question the necessity for continuous penicillin prophylaxis in rheumatic children and suggest that penicillin treatment of acute respiratory illnesses (" indicated therapy " as opposed to " continuous prophylaxis ") will achieve the same results. They compared a group of 110 children on continuous prophylaxis with a group of 103 on " indicated therapy " over a 6-year period and claim that there was no significant difference in the recurrence rates of active carditis.

[The authors' figures require very careful analysis. Editorial comment in the same journal admits that their claim is provocative but " does not yet warrant forsaking the well tested method of continuous penicillin prophylaxis ".] *A. B. Christie*

CRUICKSHANK, R. & GLYNN, A. A. **Rheumatic Fever Epidemiology and Prevention.**

This book was reviewed on p. 327.

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Anaerobes, Spirochaetes, Others.*

SMITH, G. M. **A Schick Test Survey of High School Pupils, 1958.** *Canadian J. Pub. Health.* 1960, Jan., v. 51, No. 1, 25–7.

This survey was carried out in 3 representative high schools in a rural and small urban district of Nova Scotia, with a population of 83,000 persons. The facilities for diphtheria immunization were apparently good, and there had been only 2 cases of diphtheria recognized in the period 1949–58, and none in the last 7 years.

Diluted diphtheria toxin was used for the test and diluted diphtheria toxoid for the control. The control tests were read in 24 hours and the Schick tests in 7 days. Of the 1,215 students tested, 8·5% had positive Schick tests and 3·7% had positive control tests. No person had both Schick and control tests positive.

Attempts were made to interest the parents of the Schick positive children in immunization against diphtheria, but 6 months later, according to the information received, only 21 of the 105 Schick positive children had been immunized. *H. Stanley Banks*

MARKHAM, N. P. **Diphtheria Antitoxin in the Sera of Rarotongans and in New Zealand Maoris and Europeans.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Jan., v. 54, No. 1, 47–9.

In view of the frequent occurrence of skin lesions infected with toxigenic strains of *C. diphtheriae* an investigation has been made of the antitoxin content of the sera of a group of natives of Rarotonga. The results have been compared with those obtained in the sera of groups of Maoris and white persons from New Zealand.

The result anticipated was obtained, *i.e.* Rarotongans mostly had titratable amounts of antitoxin in their sera. In comparable groups of persons over 16 years of age the Rarotongans showed only 6·5% devoid of antitoxin, the Maoris 15% and the people of European descent 78%.

The rarity of faucial diphtheria in the South Pacific is probably explained by such findings. *J. W. McLeod*

BULL. WORLD HEALTH ORGANIZATION. Geneva. 1959, v. 21, No. 3, 245–390, illustrated. [Numerous refs.] **Diarrhoeal Diseases.**

The whole of this issue is devoted to diarrhoeal diseases; there are 13 articles by authors from a variety of countries. The opening paper, *Laboratory diagnosis of Shigella and Salmonella infections*, by E. HORMAECHE and C. A. PELUFFO (pp. 247–277), is by two distinguished and very experienced bacteriologists in this field. It gives very full and detailed descriptions of the various biochemical and serological tests employed for the exact identification (phage-typing of the appropriate salmonellae is not included) of organisms belonging to the 2 groups and is little short of a monograph. As an independent contribution this article is full of interest and of considerable value, but as the opening paper to

a symposium in which exact identification of either salmonellae or shigellae plays such a small part it seems almost out of place. Many of the articles would, however, have had greater epidemiological value if they had contained more detailed information about the shigella types involved.

The second paper, *The investigation and control of salmonellosis,* by K. W. NEWELL (pp. 279–297), is an essay on epidemiological patterns of salmonella outbreaks, chains of infection and the prevention of salmonellosis in man. The essay is largely based on the author's experience in Northern Ireland and is in fact an extension of the arguments put forward in his recent paper on *Salmonellosis in Northern Ireland* [Newell *et al.* this *Bulletin,* 1959, v. 34, 670]. This is an interesting communication but it is concerned with the epidemiology of the infection rather than the diarrhoeal diseases as such.

The majority of the other papers deal more generally with the diarrhoeal diseases of infants and young children as primary bacterial infections, although other aspects are considered. For convenience they have been grouped in accordance with their titles and treated together; only a few are considered separately. While it is fully agreed that reduction of mortality of infants suffering from these conditions is of prime importance, it seems strange that a symposium of this sort should contain so little information about the bacteriology of the shigella infections.

The first group of the general papers is:—

Acute intestinal infections of non-dysenteric etiology, by E. M. LINETSKAYA-NOVGORODSKAYA (pp. 299–307). *Diarrhoeal diseases of infants and children, mortality and epidemiology,* by A. V. HARDY (pp. 309–319). *Les diarrhées infantiles en Afrique-Occidentale française,* by I. SÉNÉCAL (pp. 321–336). *A study of diarrhoea-enteritis deaths in infants in Manila, Philippines: Report of a joint study group of the Institute of Hygiene, University of the Philippines, and the Manila Health Department,* by R.-A. DAVIS, F. DEL CARMEN, R. B. ESCOSA, D. QUEBRAL-GEAGA, A. A. LIBREA, J. PORTES, JR., G. ROMAN, M. TAYBACK, A. VERGARA-VALENZUELA and V. C. VALENZUELA (pp. 337–352). *Statistics of Gastro-enteritis mortality in Venezuela,* by D. CURIEL and Elena de OCHOA (pp. 353–361). *Diarrhoeal diseases in Yugoslavia, with particular reference to Croatia,* by H. EMILI (pp. 363–367). *Les maladies diarrhéiques transmissibles du nourrisson et de l'enfant,* by R. BUTTIAUX (pp. 386–390).

Linetskaya-Novgorodskaya, an epidemiologist from Leningrad, writes interestingly about the great increase in sporadic salmonellosis among adults and the fall in the incidence of the disease in infants. Although *Salmonella typhi-murium* is the most frequently encountered member of the group it is noted with special interest that Salm. Heidelberg has recently become important [this is true also in Great Britain]. The author also draws attention to the long carriage of salmonellae after infection of young children and suggests that cross-infection from this source is probably a more important method of spread than the massive contamination of food. Experience with infantile gastroenteritis associated with *Escherichia coli* is similar to that in Great Britain except that the number of sero-types encountered appears to be more limited—0·111 is the type commonly found.

Hardy's account is probably the most valuable for he attempts, with a good deal of success, to trace the changes over the years in the mortality of these diseases throughout the world and compares the pictures seen in the economically advanced areas with those seen in the less advanced countries. In connexion with "summer diarrhoea", so widely prevalent among infants in the early years of the century, he recalls a study by FLEXNER and HOLT (1904. *Bacteriological and clinical studies of the diarrhoeal diseases of infancy,* New York) in which 66% of 421 infants hospitalized for primary infectious diarrhoea were found to be excreting Shiga or Flexner bacilli. Hardy concludes that this provides strong historical evidence that the summer diarrhoea of that time was predominantly due to shigella infections. While this may have been true in the eastern seaboard States of the U.S.A. it certainly was not true of summer diarrhoea in Great Britain over the same period. At that time, outside mental institutions, bacillary dysentery was practically unknown in the country and Morgan, who was, however, very familiar with the Flexner organisms, found only coliforms and some non-lactose fermenting types in the stools of infants suffering from summer diarrhoea. The most common of these non-lactose fermenters was known as Morgan's No. 1, now called *Proteus morgani* (MORGAN, *Brit. Med. J.,* 1906, v. i, 908), and it was found with varying degrees of frequency by a number of workers in Great Britain in cases of summer diarrhoea. After the Great War the incidence of this condition declined significantly here, but in many other countries infant enteritis continued to be a serious problem during the hot weather. In Cairo the reviewer studied a series of 526 cases among the poorer classes in the city and found, as Flexner and Holt had found some 20 years earlier in New York, that the condition was predominantly a shigella infection; the isolation figures were: Shiga 9%, Flexner 40% and Sonne 5%, salmonellae accounted for just over 1%, but Morgan's No. 1 bacillus was the predominant organism in 10% of the specimens, PERRY and BENSTED [*Trop. Dis. Bull.,* 1929, v. 26, 897]. It is also of interest to recall that HORMAECHE *et al.* [this *Bulletin,* 1944, v. 19, 341] found that among the infants suffering from acute enteritis in Uruguay some 40% were excreting shigellae and some 20% were excreting salmonella organisms; the shigellae were mainly Flexner and Sonne types. In a recent report from Dakar, BAYLET [this *Bulletin,* 1960, v. 35, 577], some of whose figures are used by Senecal in the symposium under review, showed that *Shigella dysenteria 1* (Shiga's bacillus) was still a common cause of dysentery in the area and suggested, with some reason, that it was related to the backward economical state of this area.

The remaining papers: *Prevention of mortality from diarrhoeal diseases in Brazil.* H. M. PENIDO (pp. 368–371); *Organization of the control of gastro-intestinal diseases in young children in the Soviet Union.* M. S. MASLOV and L. V. GRECHISKNIKOVA (pp. 371–374), deals with plans for the organization of child-welfare and the betterment of conditions, leading to a reduction in mortality. *Epidemiological methods used in the study of infantile diarrhoea in Israel,* by P. YEKUTIEL (374–381) adequately describes what this short note is about; it seems fairly complete and calls for no comment.

Diarrhoeal diseases and the environment. D. J. SCHLIESSMANN (pp. 381–386). This has a promising title but it deals only with water supplies, the disposal of excreta and the fly as a transmitter of infection. The contamination of the general environment with infected material, which is probably the most important aspect, is not considered.

While there can be no doubt about the effect of nutrition, child-welfare organization and other factors of this nature on the reduction of the death rates from the diarrhoeal diseases of infancy in the economically advanced countries, it is extremely difficult to judge their effect on morbidity or indeed to obtain accurate figures relating to the overall incidence of these diseases even in the most advanced countries where the condition may be clinically so mild as to escape attention.

Although there are good reasons for assuming that the condition is always infective (accepting the part played by protozoa and other agents under this heading), it is often not possible to identify the infecting agent in the very young infant. In spite of the reluctance in some quarters to accept the highly infective enteropathogenic strains of *Escherichia coli* as primary causes of infant diarrhoea, their importance in the most highly developed countries is steadily being established. In the less economically advanced areas in the world these strains are not well established as potentially causative organisms of infant diarrhoea; indeed in many such areas the various members of the shigella group are clearly implicated. Flexner organisms are most commonly isolated, but it must not be forgotten that in certain areas, that are regarded as economically undeveloped, Shiga dysentery is not infrequently seen [see report by Baylet from Dakar, *loc. cit.*]. Nevertheless, the virtual disappearance of Shiga dysentery from most areas of the world is truly remarkable; it is only equalled by the no less remarkable increase in the incidence of Sonne dysentery in many of the most economically advanced countries. It is of particular interest to note that in the U.S.S.R., where Shiga's bacillus used to be a common cause of infant diarrhoea, this type of infection is now infrequently seen in the cities, but Sonne dysentery has become increasingly common in child-welfare clinics and other institutions [ZHDANOV, *ibid.*, 1959, v. 34, 1239].

H. J. Bensted

FROMME, W., TRÜB, C. L. P. & POSCH, J. Zur Epidemiologie des Typhus und Paratyphus mit besonderer Berücksichtigung der Ermittelung der Dauerausscheider. [**Epidemiology of Typhoid and Paratyphoid Infections—Ascertainment of Chronic Carriers**] *Öffentl. Gesundheitsdienst.* Stuttgart. 1960, Feb., v. 21, No. 11, 460–65, 1 fig.

In the period 1950–57 the incidence of the enteric fevers in North-Rhine-Westphalia has diminished from 1,725 to 714 cases of typhoid fever and from 1,650 to 696 cases of paratyphoid fever. The factors which have played a part in this reduction are discussed. Most of the paper is devoted to an account of the methods, officially introduced in 1948–49, for the ascertainment and control of chronic bacterial carriers. There are also some particulars of the length of the time that elapsed between the beginning of illness and admission to hospital, the period of treatment in hospital and the cost of this treatment and the seasonal distribution of cases of these infections.

M. E. Delafield

COLLARD, P., SEN, R. & MONTEFIORE, D. **The Distribution of *Salmonella* Agglutinins in Sera of Healthy Adults at Ibadan.** *J. Hygiene.* 1959, Dec., v. 57, No. 4, 427–34, 2 figs. [20 refs.]

This survey of the agglutinin levels in healthy West Africans covers the most important salmonella O-antigen complexes and also the most important H antigens and attempts to relate these findings to the antigens of the various salmonella serotypes routinely isolated from the stools and other sources of patients in hospital or attending the out-patient department. Although there was a good deal of agreement between what was accepted as a significant level of agglutinins to the various antigens and the distribution of the salmonella serotypes (there were 78 different species), there were some outstanding differences. For example, agglutinins to O-antigen factors 3,10 were extremely common whereas the isolations of salmonella types with this O-antigen formula did not match with this. While the observations recorded in this paper have some interest their significance seems to be doubtful.

H. J. Bensted

SCHIMIZZI, M. & VINGIANI, A. Pleuro-pneumopatie in corso di febbre tifoide. [**Pleuro-pneumonia occurring during Typhoid Fever**] *Acta Med. Italica.* 1959, Feb., v. 14, No. 2, 42–8, 18 figs. [13 refs.]

The authors point out that pleurisy, pneumonia, or bronchopneumonia can occur during enteric fever, that the pleurisy can be dry, serohaemorrhagic or purulent and that fleeting manifestations can be detected radiologically in the lungs although beyond a few sibilant sounds there is nothing else to suggest that the lung is involved. These changes are mainly due to the usual bacterial flora of the respiratory tract, but specific pleuropulmonary changes due to *Salm. typhi* do occur.

7 cases are described of radiological changes in the lungs and pleurae in patients who had an acute illness all had faeces positive for *Salm. typhi* and all had an O agglutinin titre of at least 1:80. Only 1 patient was over 16 years of age. Chest X-rays showed some temporary shadowing mainly of the hilar regions and in the lower lobes which disappeared quite rapidly on treatment of the general disease. The authors consider that these manifestations are more frequent in typhoid than is generally imagined and that they may well suggest a commencing tuberculous condition. The pathogenesis is uncertain but it may possibly be of allergic origin though eosinophilia was not present.

W. K. Dunscombe

BRANCACCIO, G. & VINGIANI, A. Su un caso di febbre tifoide caratterizzato da CAF-resistenza del ceppo di *S. typhi* responsabile della malattia. [**Typhoid Fever due to a Chloramphenicol-Resistant Strain of *Salm. typhi***] *Acta Med. Italica.* 1959, Mar., v. 14, No. 3, 75–80. [46 refs.]

A 60-year-old man having a 3 months' history of feeling out of sorts, lack of appetite, and some fever during which on the advice of his doctor he took chloramphenicol 1·5 gm. daily for 9 days, was eventually admitted to the medical wards of a hospital where after repeated negative Widal and faeces cultures finally an H and O titre of 1:40, Vi 1:16 for *Salmonella typhi* was obtained and the organism was recovered from the stools, the patient's serum agglutinating it to 1:2560. Treatment by chloramphenicol 1·5 gm. and prednisone 20 mgm. daily was ineffective as also were intravenous vaccines. It was then found that for the strain isolated the minimum inhibitory concentration of chloramphenicol was 16 μgm., but that it was very sensitive to streptomycin. Accordingly treatment was restarted with chloramphenicol 1·5 gm. and streptomycin 1 gm. daily (2 x 0·5 gm. every 12 hours). The patient then recovered and remained quite well.

The authors emphasize (1) the relatively mild course in a man 60 years of age, (2) the diagnostic value of Duguet's ulcer of the anterior fauces, (3) the resistance of the strain of *Salm. typhi* to chloramphenicol and its sensitivity to streptomycin. They suggest that since chloramphenicol treatment did not begin until at least 15 days after the illness started the structure of the organism could not have been modified by the drug, at least initially. They consider that the stock suspension for the Widal and the stock vaccine for treatment lacked the requisite stimulus in this case. They then ask if there was any relationship between the resistance of the strain, the results of the Widal and of vaccine therapy, and the mildness of the disease, and concluded that there was. *W. K. Dunscombe*

Ruiz Sanchez, F. & Naranjo Granda, E. **Combined Phenylbutazone and Tetracycline in the Treatment of Typhoid Fever.** *Antibiotic Med.* New York. 1959, Sept., v. 6, No. 9, 537–44, 3 figs. [13 refs.]

Very good results are reported in 17 moderately severe cases of typhoid fever and 1 severe case treated with a combination of phenylbutazone (Butazolidin) and tetracycline. The results were only slightly inferior to those reported in 1958 by the authors with a combination of phenylbutazone and chloramphenicol [this *Bulletin,* 1959, v. 34, 205]. The temperature was used as the criterion to indicate the results of treatment—"very good" when the fever disappeared in 24–36 hours, "good" when it disappeared during the first 3–5 days of treatment (as it frequently does when chloramphenicol alone is employed), "incomplete" when the fever disappeared later but before the end of therapy, and "unsatisfactory" when it did not disappear until after the end of therapy. The results, as thus assessed were "very good" 15 (83·3%), "good" 2 (11·7%) and "unsatisfactory" 1 (5·8%). Coincident with the fall in temperature to normal there was general improvement, with reduction or disappearance of stupor or delirium, feeling of well-being, and prompt return of appetite.

[This article is difficult to evaluate. Phenylbutazone has no *in vitro* antibacterial action against *Salm. typhi.* The good effects are attributed to its antipyretic and anti-inflammatory actions; these, it is postulated, potentiate the antibiotic to give *clinical* results superior to those obtainable with the antibiotic alone. The immediate bacteriological results were not good; blood cultures were still positive in some cases on the 5th and 6th day of treatment, that is when the temperature had been normal for some days—an extraordinary result which could only be associated with some artificial reduction of the temperature. There is no report on stool cultures in this article—a notable weakness. No complications, relapses, or deaths, however, occurred. Phenylbutazone is a toxic drug, but only occasional vomiting was reported in this series.] *H. Stanley Banks*

See also p. 653, Cameron, **A Localized Outbreak of Paratyphoid B Fever (Phage-Type Taunton).**

Serova, L. A. **The Effect of Prophylactic Vaccination on the Course of Paratyphoid B.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 4, 83–7, 3 figs. [Translated from Russian.]

This author brings forward evidence to show that enteric fever in the vaccinated person is a much milder clinical illness than that seen in the unvaccinated control. The author is obviously aware that there is, in the literature, opposition to this thesis, but she brings forward no valid statistical evidence to prove that prophylactic vaccination with typhoid-paratyphoid vaccines influences the clinical course of enteric fever in patients who may subsequently contract such an infection. *H. J. Bensted*

McGregor, A., Fairlamb, A. H. & Hutchison, A. **A Family Infection due to Salmonella Abony.** *Med. Officer.* 1959, Dec. 24, v. 102, No. 26, 329–30. [12 refs.]

The illness of a child aged 6 months with acute diarrhoea and vomiting led to the isolation of Salmonella Abony from both parents and 2 sisters (3 and 5 years), only the father admitted symptoms of abdominal pain and vomiting 2 weeks before the child's illness; 2 of 6 members of the grandmother's household visited by the infected family also suffered from gastro-enteritis at the same time but all stool samples were negative. 1 of 3 tortoises from the vicinity was excreting Salm. Potsdam and Salm. Rubislaw [this *Bulletin,* 1953, v. 28, 856].

The source of Salm. Abony was not found.
Betty C. Hobbs

De La Torre, J. A. & Olarte, J. **Synnematin B in the Treatment of *Salmonella* Enteritis in Infants.** *Antibiotic Med.* New York. 1959, Dec., v. 6, No. 12, 724–30.

This is a preliminary, and inconclusive, report on the treatment with synnematin B of 10 infants suffering from *Salmonella infection* (5 *Salm. typhimurium,* 3 *Salm. oranienburg,* 1 *Salm. infantis,* and 1 *Salm. paratyphi B*).

All the infants were malnourished, and had had symptoms for 10 days to 3 months before this antibiotic was given; 6 of them had also had previous treatment with chloramphenicol or tetracycline. The organism was recovered from the stools in 10, and also from the blood in 5. All the organisms recovered were sensitive to 2 units/ml. synematin B, except the *Salm. infantis* which was resistant to 50 units/ml.

The results in this unpromising series were inconclusive, although the dosage was extremely high. There were 3 apparent clinical and bacteriological cures, and the remainder were unchanged or had a doubtful result.

H. Stanley Banks

SPINK, W. W. **Current Status of Therapy of Brucellosis in Human Beings.** [Report to the Council on Drugs (KAUTZ, H. D., Secretary).] *J. Amer. Med. Ass.* 1960, Feb. 13, v. 172, No. 7, 697–8.

The author presents a well balanced view of the treatment of brucellosis. The first consideration should be with respect to an accurate diagnosis. Too many people in whom active disease is not demonstrable are subjected to treatment. In general, agglutination titres of 1:100 or over are consistent with active disease. The brucella skin test only indicates past exposure. Infections due to *Brucella abortus* tend to be less severe than those due to *Br. melitensis* or *Br. suis*.

The author advocates 500 mgm. orally of a tetracycline drug every 6 hours for a minimum of 21 days, repeated within 6 to 8 weeks if a relapse occurs. In the more severe cases 1 to 2 mgm. of streptomycin intramuscularly should be given daily for 14 days simultaneously with the oral tetracycline.

Patients exhibiting a severe toxic state should be given steroid therapy in addition for the first 24 to 72 hours only. This may be given as corticotrophin 40 mgm. intramuscularly every 8 hours, or orally as cortisone acetate (100 to 300 mgm.) or prednisone (20 mgm.) 3 times daily. Relief of severe toxic symptoms occurs within 24 hours instead of over several days as achieved by antibiotics alone.

The treatment of the occasional patient who relapses may necessitate a third course of tetracycline for 21 days. It is doubtful whether more than 3 courses should be given except in the rare patient in whom demonstrable suppuration is present.

So-called chronic brucellosis may be an aftermath of brucellosis in an emotionally unstable person and does not then call for further antibiotics. Brucella vaccines have been used, by parenteral injections, in an attempt to desensitize patients to brucella antigen. It is difficult to evaluate the success of this disturbing treatment. The intravenous use of vaccines for the acutely ill patient is dangerous and should not be employed.

[The author does not here present statistical evidence, or refer to the possible advantage of adding sulphonamides to the antibiotics. No reason is given for omitting streptomycin in the treatment of relapses. The place of steroids in therapy is well presented. In considering the doubtful case agglutinins produced by cholera vaccination should be remembered.]

Frederick J. Wright

OLITZKI, A. L., SULITZEANU, D., ARNAN, A. & RASOOLY, G. **Observations on Men Vaccinated with a Streptomycin Dependent *Brucella* Strain.** *J. Infect. Dis.* 1960, Jan.–Feb., v. 106, No. 1, 77–82.

A living brucella vaccine prepared from the attenuated streptomycin-dependent strain of *Brucella abortus*, 19D, was given to 80 persons living in a village with a high incidence of brucellosis. The dose was 2 x 10^8 organisms. Great care was taken to exclude those with clinical brucellosis and also, as far as possible, those with sub-clinical infections, in order to prevent undesirable reaction. Nevertheless 14 persons reacted strongly to the living vaccine and it found that 4 of them were suffering from brucellosis; the others were judged to be latent cases. Among the remainder 80% showed significant rises in agglutinin titres and these sera also showed a positive protective index, as measured in mice, and 40% gave positive intradermal tests.

Although further cases of brucellosis were not seen in this village it was not possible to say whether the immunization of the villagers with the living vaccine was responsible because the health authorities initiated certain control procedures at the same time.

H. J. Bensted

HOPLA, C. E. **The Transmission of Tularemia Organisms by Ticks in the Southern States.** *Southern Med. J.* 1960, Jan., v. 53, No. 1, 92–7, 4 figs. [19 refs.]

The majority of human cases of tularaemia in the southern states of the U.S.A. occur in the first 2 quarters of the year, followed by a slight drop in the third quarter and the smallest number in the fourth. This seasonal incidence differs from other regions of the United States. Several ticks have been shown to act as vectors of tularaemia and of these the distribution of the lone-star tick, *Amblyomma americanum*, closely follows the area of the southern region of the United States.

The author conducted experiments designed to indicate what part *A. americanum* may play in determining the peculiar seasonal incidence of tularaemia in the southern states. It was found that this tick forms 90% of the tick population during the spring and summer months, the American dog tick, *Dermacentor variabilis* being the next most frequent then of the other ticks which attack man; the black-legged tick, *Ixodes scapularis*, is abundant from October to February. The rabbit tick, *Haemaphysalis leporis-palustris*, is prevalent throughout the year and is important as a vector among rabbits. *A. americanum* is a 3-host tick and may feed on man in any of its 3 stages which, together with transovarian transmission, enhances the likelihood of human infection. Observations by BELL [this *Bulletin*, 1946, v. 21, 101] on *D. variabilis* infected with *Brucella tularensis* have shown that during its feeding on immune or normal hosts this tick loses its infection with *Br. tularensis*, presumably as the result of the bactericidal effect of the ingested blood even though the susceptible host may develop tularaemia. Feeding experiments carried out by the author indicate that *A. americanum* does not lose its infection with *Br. tularensis* when feeding on immune animals. Furthermore

it was shown that the number of organisms retained by the tick depends on the stage of the life cycle and the length of time since the tick had a blood meal, but that fasting ticks, with a reduced number of organisms, are still efficient vectors. The importance of the nymphal stage of *A. americanum* in producing tularaemia in man is not known but there are indications that the tick at this stage has infected man. *Frederick J. Wright*

TAKIZAWA, T. **Epidemiological Studies on Yato-Byo (Tularemia in Japan) in Nagano Prefecture. I. On the Mass Survey by Yato-Byo Skin Test and on the Specificity of the Test.** *Fukushima J. Med. Sci.* 1959, Mar., v. 6, No. 1, 1–15, 1 diagram. [12 refs.] **II. On the Dose of Skin Test Antigen.** *Ibid.*, 17–21.

I. Further observations on skin testing in relation to tularaemia are reported. Analysis of the results obtained among 8,390 persons in the Nagano Prefecture indicated that induration gives a more reliable indication of a specific response than erythema alone and that an indurated area over 10 mm. may be considered as a positive reaction; 8–9 mm. as doubtful. This is also in agreement with the findings in Japan of SASE [this *Bulletin*, 1959, v. 34, 890]. Comparison of the results obtained by the use of the tularaemia antigen, a suspension of the Ebina strain of *Brucella tularensis* (called Yato-byo bacillus) and on the reaction to histoplasmin suggests that induration to the last of a diameter less than 5 mm. should be considered to be a non-specific reaction.

II. Preliminary observations had suggested that the intradermal injection of 0·05 ml. of the tularaemia antigen might give more reliable results than injecting 0·1 ml. This was further assessed by testing 705 schoolchildren simultaneously with both quantities (0·1 ml. in the right forearm, 0·05 ml. into the left). Less erythema and induration were produced by 0·05 ml. than 0·1 ml. and the induration only exceeded 10 mm. in diameter in 1 case from the smaller injection and this child showed an agglutination titre of 1:64. Areas of induration less than 10 mm. in diameter were produced in 56 from 0·1 ml. but in only 8 from 0·05 ml. It is concluded that with the smaller dose of 0·05 ml. induration is a better indication of a specific response than when 0·1 ml. is used. It is also suggested that it may be better to read the result 72 hours after the injection instead of 48 hours but that further observations are required to confirm this.

[In the second group of observations only 1 schoolchild showed clear evidence of having been infected with tularaemia, thus the conclusions are based primarily on the evidence pointing to presumed non-specific reactions. 0·1 ml. is erroneously printed as 0·01 ml. in paragraphs 2 and 5 of the summary in the second paper.]
Frederick J. Wright

PETRILLA, A. **Results of Active Immunization of Civilian Population against Tetanus.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 1, 65–70, 1 fig.

"In Hungary vaccination against tetanus was made compulsory in 1953. Since then children have been vaccinated in the second half year of life, and at 6 years of age, with diphtheria-pertussis-tetanus combined vaccine, finally, at 12 years of age with typhoid-tetanus combined vaccine. At each instance two inoculations are given at an interval of four weeks, and basal immunization is followed by a booster dose one year later. In 1958 the age group under 20 years might be regarded as vaccinated. For the vaccinated age group the tetanus morbidity rate, which amounted to 9·2 per 100,000 before the introduction of vaccination (average for 1951 and 1952), has decreased by 80% to 1·7 per 100,000 (rate for 1958). Thus, in spite of the fact that from 5 to 10% of the children have escaped compulsory vaccination, the results are satisfactory. The decrease in the incidence of neonatal (under one year of age) tetanus is attributable to other factors, *e.g.* to the substantial rise in institutional confinements. Another possible factor is that certain mothers, chiefly the younger ones, have been immunized. We failed exactly to establish the vaccination status of the tetanus patients. Eighty-five per cent of the injuries leading to tetanus were too mild to be shown to a doctor. In such cases active immunization is the only means of preventing tetanus."

HOUBA, V. Zur äthiopathogenetischen Therapie der experimentellen Gasgangrän-Infektion. [**On the Aetiotropic Therapy of Experimental Gas Oedema Infection**] *Zent f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 605–17, 1 fig. [52 refs.]

The relative value of serum therapy administered by various routes is discussed, and its combination with antibiotics.

It is claimed that in view of the importance of the lymphatic channels in the absorption of toxin, which was demonstrated, the administration should take the form of specific blockade, *i.e.* introduction of anti-serum to the muscles of the affected limb between the lesion and the heart. The observations were made on rabbits in the limbs of which gas gangrene was set up by muscle damage with insertion of sand and clostridial culture, and these showed that the "blockade" therapy with anti-serum was better than intramuscular injection in other sites and equal to intravenous injection. The best results, however, were obtained by combining chlortetracycline 20 mgm./kgm. of body weight, with "blockade" serum therapy. Penicillin was less effective in combined therapy. It was, however, only tried in doses of 16,000 units/kgm./24 hours. *J. W. McLeod*

ŠEBEK, Z., JANÍCEK, B. & ŠULA, V. Epidemie Weilovy choroby v jihlavě na jaře 1958. [**Epidemic of Weil's Disease in Jihlava in Spring 1958**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 2, 126–34.

The English summary appended to the paper is as follows:—

"The authors describe an epidemic of Weil's disease which occurred in Jihlava in spring 1958. The infection spread from a closed swimming pool into which rats penetrated. Serologically by means of the MAL reaction with 12 strains of leptospira a total of 136 individuals

were examined. Antibodies against L. icterohaemorrhagiae were found with a titre of 1:400 and above in 37 individuals. Two patients did not bathe in the swimming pool but worked in the close vicinity of the pool. The water in the swimming pool was infected for cca five weeks. For the disinfection Sagen was used in amounts corresponding to one third of the recommended dose. Under experimental laboratory conditions the authors revealed that the recommended doses of Sagen did not kill the cultures of L. icterohaemorrhagiae even after a week. The clinical course of the epidemic was mild. Seventeen patients were admitted to hospital, four were treated at home, 18 persons with serologically positive reactions lacked clinical symptoms. The authors give a brief account of the clinical symptoms, results of laboratory tests and treatment. It did not prove possible to isolate the pathogenic agent from the blood and urine of the patients. From a rat caught in the vicinity of the swimming pool the strain L. icterohaemorrhagiae was isolated. A total of 55 rats was examined, inc. 19 with positive serological reactions and six which were positive on cultivation. All isolated strains were identified as L. icterohaemorrhagiae. The authors demand a more strict sanitary control of swimming pools and recommend the use of chlorine preparations for disinfection."

BULL. INST. HYG. Belgrade. 1959, v. 8, No. 3, 1–79, 2 maps & 1 fig. [Numerous refs.] [In Serbian.] English summaries 81–6. [**The Problem of the Chronic Nephritis in Serbia**]

A high incidence of chronic nephritis has been known to exist along certain river systems in Serbia, in one place involving one-third of the population, and affecting females more than males at all ages except over 50 years. The lowest rates were in children. Several papers in this issue of the *Bull. Inst. Hyg.* of Belgrade are devoted to the subject, but the results of investigations are inconclusive. Lead poisoning was suspected but no evidence of it was found. In the final paper it is shown that leptospire antibodies were found in 43·8% of domestic animals examined and that in the households with high animal rates the same antibodies were common in the human populations. *Charles Wilcocks*

KAIJSER, K. & MALMSTRÖM-GROTH, A. Listeriosis—ytterligare fall hos spädbarn. [**Listeriosis—Further Cases in Infancy**] *Svenska Läkartidningen.* 1960. Mar. 11, v. 57, No. 11, 792–5. [11 refs.]

Detection of cases of listeriosis in various parts of Sweden, chiefly in its larger towns, has yielded a veritable crop of original articles on it in the Scandinavian medical press in 1959 and 1960. The table in which these already published articles are presented shows that most of the patients were not yet born or were premature infants at birth. The clinical picture was usually that of septicaemia or meningitis, and the mortality was high. The sudden appearance of so many cases in different parts of Sweden raised the question whether they reflected diagnostic awareness in the medical profession or the actual spread of the disease from the large towns to other parts of the country.

The case on which the present article hinges was that of a female born a fortnight before the expected birth and weighing 3·050 gm. The rash for which she was admitted to hospital yielded a growth of *Bacillus subtilis.* Discharged as cured, she was re-admitted to hospital a fortnight old with fever and general malaise. The cerebrospinal fluid showed total protein 1·024 mgm.%, 5,300 cells, mostly polynuclears and a few Gram-positive rods. A Swedish culture was sent to Professor SEEGER in Bonn where *Listerella monocytogenes* type I was found. Treatment with various antibiotics was followed by some improvement, with return of the cerebrospinal fluid to normal. But hydrocephalus set in and the infant was 65 days old when she died. *Post mortem,* no growth of *Listerella* was obtained from the brain, cerebrospinal fluid or intestines. *Claude Lillingston*

HARTER, D. H. & PETERSDORF, R. G. **A Consideration of the Pathogenesis of Bacterial Meningitis: Review of Experimental and Clinical Studies.** *Yale J. Biol. & Med.* 1960, Feb., v. 32, No. 4, 280–309. [218 refs.]

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lymphogranuloma group; Pox group; Repiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.*

LIU, C. **The Use of Fluorescent Antibody in the Diagnosis and Study of Viral and Rickettsial Infections.** *Ergebn. Mikrobiol. Immunitätsf.* 1960, v. 33, 242–58, 7 figs. [Numerous refs.]

This paper, enhanced by 6 good photomicrographs and a full bibliography, reviews the results so far obtained in studies on the usefulness of the fluorescent antibody technique in various immunohistochemical problems in the diagnosis of several viral and rickettsial diseases. The author summarizes the work of COONS and his colleagues on the technical procedures involved and enumerates the findings in mumps, influenza and fowl plague, adenoviruses, primary atypical pneumonia, psittacosis, varicella and herpes zoster, vaccinia, Egypt 101 virus, poliovirus, Teschen disease virus (virus encephalomyelitis of swine), canine distemper, viruses that produce inclusion bodies (herpes simplex, canine distemper, canine hepatitis and rabies), miscellaneous viruses (Newcastle disease virus, Shope papilloma virus, measles and simian foamy agent) and rickettsiae. [Readers should refer for the details to the original paper (which is in English).]

The author concludes that the fluorescent antibody technique has been proved very useful, especially when morphological localization of antigens in tissues is in question; one of the great advantages of the technique is the precise localization of antigens at the cellular level. When used in conjunction with other virological techniques, the fluorescent antibody technique can lead to the development of intelligent rapid diagnostic methods. *D. A. Cannon*

CANCELLARA, E. La diagnosi precoce del vaiuolo el il segno del Gasperini. Note sulla epidemia di vaiuolo in Bari (Novembre 1945–Marzo 1947). **[Gasperini's Sign in the Early Diagnosis of Smallpox. Note on the Epidemic in Bari from November 1945 to March 1947]** *Igiene e San. Pubblica.* Rome. 1959, Nov.–Dec., v. 15, No. 6, 526–33, 2 figs. English summary (9 lines).

According to the author Gasperini's sign consists in the absolute lack of spots in the 2 lower quadrants of the abdomen in varicella, which distinguishes it from variola. [GASPERINI'S own words, translated from *Arch. Ital. Sci. Med. Colon.*, 1937, v. 18, 421, are, "The sign which has been found constant in all cases of varicella is the complete absence of pustules in the two inferior quadrants of the abdomen."] Cancellara mentions that of 85 patients seen at the paediatric clinic during the epidemic Gasperini's sign was found in 63 and was absent in 22. All 85 were subsequently diagnosed as smallpox but in those 22 who were negative, the clinical course was particularly benign.

As for the epidemic itself, 185 cases were notified during the period and the outbreak is regarded as having arisen from a mild undiagnosed case in a girl who came to town from Naples where an epidemic was in progress. Of the total number 137 had never been vaccinated and only 39 were over 10 years of age. 4 patients died.

[The low case fatality rate among so many unvaccinated children is surprising.] *W. K. Dunscombe*

USHER, G. S. **The Feasibility of Smallpox Eradication.** *Pub. Health Rep.* Wash. 1960, Jan., v. 75, No. 1, 37–42, 2 figs.

"A proposal that the World Health Organization undertake a program of worldwide smallpox eradication is under study at the present time. The feasibility of such an undertaking under presently existing circumstances is dependent on the likelihood of success in countries where eradication is likely to be most difficult to accomplish and the obstacles greatest. One of these countries is Pakistan, in whose Eastern Province smallpox is deeply entrenched as an endemic and epidemic disease.

"In 1958 a team of epidemiologists from the Communicable Disease Center of the Public Health Service was assigned to the International Co-operation Administration to participate in the assistance that the latter was extending to the Government of Pakistan in combating a smallpox epidemic in East Pakistan. Some of the observations of this team are pertinent to the question of whether it would be feasible at this time to attempt the eradication of smallpox in the Province.

"It is concluded that such an undertaking is feasible at this time if certain problems are recognized and successfully dealt with. The concept of 'density of susceptibles' is postulated, and certain other factors bearing on the problem are discussed. It is suggested that the strategic plan would need to be the same one that has led to the eradication of smallpox elsewhere, namely, reduction of prevalence by means of widespread vaccination, followed by surveillance and emergency containment of each outbreak as it occurs. For the latter it is believed that primary reliance should be placed on 'area containment' rather than 'ring containment.'"

KALRA, S. L. **Revaccination against Smallpox with Calf Lymph and Vaccinia Virus grown on Chick Embryos.** *Indian J. Med. Sci.* 1960, Feb., v. 14, No. 2, 122–9, 1 fig.

The object of this exercise was to estimate the level of antibodies in certain recruits on joining the Indian Army and the effect on this level of vaccination with either calf lymph or egg-cultured vaccinia virus.

For antibody estimation the haemagglutination inhibition (HAI) test alone was used. Results of the vaccinations were recorded as "no reaction", "modified reactions", or "takes". For details of the results of the study the original paper must be consulted, but the author's main conclusions appear to be the following: (1) Both types of vaccine were equally effective; (2) The chance of a rise in HAI titre was greater when the interval between vaccinations was long or when the initial titre was low; and (3) Loss of immunity to vaccinia in most, but not in all, cases was a slow process.

[In criticism it may be said that the haemagglutination-inhibition test is not necessarily a reliable index of immunity against vaccinia or smallpox; and it is highly probable that among the reactions classified as "modified" some purely sensitivity reactions must have been included.] *J. Pickford Marsden*

MORRIS, J. A. & NAKAMURA, K. **Recovery of Herpes Simplex, Spontaneous Murine and Chick Viruses in Tests on Specimens from Infectious Hepatitis Patients.** *Amer. J. Trop. Med. & Hyg.* 1959, Nov., v. 8, No. 6, 723–8.

In an attempt to isolate the causative agent, throat washings, stools and serum from 200 young adults in hospital with infectious hepatitis were inoculated into cultures of 4 human cell lines (bone marrow, liver, intestine and conjunctiva), and into suckling mice, chicks and eggs. 12 strains of murine hepatoencephalitis and 5 of ectromelia were picked up in mice, in which they were known to be enzootic. 4 agents which caused macroscopic liver lesions in chicks were isolated. None of these agents reacted with antibodies in paired sera from the patients and they were clearly contaminants. No viruses were isolated in chick embryos.

The only virus isolated in the cell cultures was herpes simplex. This was recovered from 7 patients, who possessed high levels of antibody and in whom the virus was apparently latent. A rise in antibody was found, however, in sera from 5 other patients who were evidently experiencing primary infection with herpes at the same time as infectious hepatitis, but no virus was isolated from them. It is thought that the infections occurring simultaneously were independent.

[It is remarkable that no other viruses at all were recovered from such a large number of young adults. The authors state that enteroviruses were being isolated in the same laboratory routinely and that the throat, intestine and blood of these patients appear to have been free of viruses.] *Janice Taverne*

MULDER, J. & MASUREL, N. **The Epidemiology of Pandemic A2 Influenza in the Netherlands, 1957–58.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 399–407, 8 figs. [17 refs.]

"The virus of pandemic A2 influenza was introduced into the Netherlands by ship and aeroplane from Indonesia and possibly also from the Near East, causing an epidemic of 10 months' duration. The disease spread from two probably independent foci: Bussum and Rotterdam. Three special population groups were attacked first: 70 Ambonesian camps, Army units and the mining district. The main community-wide outbreak started in September 1957 and subsided in November, but cases continued to occur until April 1958 and there was a recrudescence of the disease in January and February 1958. Morbidity was highest among children and adolescents. The mortality rate amounted to about 1 in 3,700 inhabitants."

VANREENEN, R. M., ELISBERG, B. L., WEBB, P. A., TRAUB, Renee G. & TRAUB, R. **Asian Influenza in the Army in Malaya in 1957.** *J. Roy. Army Med. Corps.* 1960, Jan., v. 106, No. 1, 12–21, 2 figs.

Asian influenza first appeared at the end of April 1957 in a Gurkha infantry battalion which had recently arrived in Malaya from Hong Kong; this occurred about one week before influenza was first reported in Singapore. The infection had probably been acquired in Hong Kong, although *epidemic* influenza was not reported there until some days after the battalion had left. The interval of 19 days between the departure of the Gurkhas from Hong Kong and the eruption of the epidemic in the battalion, was almost the same as that preceding *epidemic* influenza in Singapore and Malaya, and was in contrast with the subsequent very rapid spread among communities in Malaya. These facts seem to support the theory that influenza virus may be introduced and widely seeded in a community before it gives rise to an epidemic [ANDREWES, this *Bulletin,* 1954, v. 29, 449].

7 strains of influenza virus isolated from Gurkha and Malayan patients were shown to be closely related to the type strain A/Singapore/1/57. The maximum antibody response to infection with this virus occurred about 28 days or more after the onset of clinical symptoms. The clinical attack rate among Asian soldiers was 32% and among Europeans 9%; while haemagglutinin-inhibition tests on single sera collected at the end of the epidemic showed that 39% of the Asian soldiers who had remained symptom-free had been infected with the virus, compared with 7% among the symptom-free Europeans. No satisfactory explanation of this wide difference in infection rates between Asian and European soldiers is offered.

H. Stanley Banks

COOK, M. K., CHANOCK, R. M., FOX, H. H., HUEBNER, R. J., BUESCHER, E. L. & JOHNSON, R. T. **Role of Eaton Agent in Disease of Lower Respiratory Tract. Evidence for Infection in Adults.** *Brit. Med. J.* 1960, Mar. 26, 905–11. [28 refs.]

The role played by the Eaton agent [EATON *et al.*, this *Bulletin,* 1944, v. 19, 906] in the aetiology of primary atypical pneumonia was investigated in adults with or without cold or streptococcus MG agglutinins or both and in children with lower respiratory disease. Antibody rises to the Eaton agent were detected by the fluorescent antibody technique [this *Bulletin,* 1959, v. 34, 988] in 22 of 26 adult patients with rises in cold or streptococcus MG agglutinins or both and in 18 of 69 patients who failed to develop these agglutinins. Eaton antibody rises were also found in 18 of 110 children with lower respiratory disease not associated with other known respiratory viruses. No antibody rises for the Eaton agent were detected among 64 children free of respiratory illness. Virus strains serologically identical with the Eaton agent were isolated from sputum specimens of 2 adult patients by amniotic inoculation into 13-day fertile eggs. One of these 2 strains was also isolated by intranasal inoculation into mice.

The specificity of the fluorescent antibody technique for the detection of Eaton-agent antibodies was confirmed by the uniform failure to demonstrate rises of these antibodies in sera from adults infected with para-influenza 1, para-influenza 3, Asian influenza, adenovirus, Q-fever and psittacosis virus.

H. G. Pereira

REALMUTO, A. & SCOZZARELLA, E. La poliomielite in Italia e le manifestazioni epidemiche nel 1958. **[Poliomyelitis and its Epidemic Manifestations in Italy during 1958]** *Ann. d. San. Pubblica.* Rome. 1959, Sept.–Oct., v. 20, No. 5, 879–936, 14 figs. (3 coloured on 3 pls.). [35 refs.] English summary.

In compiling their figures and graphs and many of their tables for this statistical study, the authors have considered the presumed date of onset rather than the date of notification—the latter is the basis of official bulletins and returns.

The records of the disease in Italy go back to 1924, but an unknown number of cases will have remained unreported, more especially in the first decade of this 34-year period. Because of war conditions, reporting will also have been defective for 1942–45. With 8,394 notifications of paralytic cases in 1958, the incidence rate for that year was 16·7 per 100,000 and far higher than for any of the previous known years. There were 1,173 deaths—a death rate of 2·34 per 100,000 and a case mortality rate of 14%—also a record. The graphs show peaks of incidence rate in 2 previous years —1939 and 1953, with rates of 13·7 and 10·5 per 100,000 respectively. There has been a progressive rise to the record incidence of 1958, the rate having been 7·1 in 1956 and 9·0 in 1957. Most cases in 1958 occurred in the latter part of the year and there is a steep peak in October; previous years had shown an aestivo-autumnal seasonal distribution and summer had been the epidemic season. The geographical distribution is discussed and illustrated with coloured maps: southern provinces, including Rome, had the highest incidence rates. The epidemic started in the Naples area—at Frattamaggiore and Afragola.

7,114 cases were children aged up to 4 years, 2,280 in the first year of life. Infants should be given polio vaccine in the 3rd, 4th and 5th months of life, with a fourth dose 7 to 8 months later. The immunization of pregnant women might also be considered, to protect the offspring. There was no evidence yet of a shift of incidence towards adult age-groups in Italy. *J. Cauchi*

PROVVIDENZA, G., MARIONI, R. & CARUSO, A. Considerazioni epidemiologiche, cliniche e statistiche su 2053 casi di malattia di Heine-Medin. [**Epidemiological, Clinical and Statistical Data on 2,053 Cases of Poliomyelitis**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1959, Nov., v. 40, No. 11, 623–30, 3 graphs. [37 refs.] English summary (9 lines).

The authors have studied the records of cases of poliomyelitis seen in the Infectious Diseases "Clinic" of the University of Rome from 1947 to October 1959: 1,168 were male patients and 885 female. Until 1957, children of 2 to 3 years suffered the highest incidence; in 1958 and 1959, the age-group of highest incidence included the first and fourth years. Most cases occurred in the 3 months from July to September, and a graph shows that the incidence begins to rise in February and is progressive from then on. Numerous theories have been suggested to explain the seasonal distribution.

205 of the 2,053 patients (10%) died, but the case mortality has recently risen: there were 138 deaths among 746 cases (18·5%) in 1958; and during this year many more cases were severe with bulbar, cerebral and meningeal involvement.

There has been a drop in incidence and in case mortality for 1959, and it is suggested that there may be some connexion with the immunization drive which is taking place over the whole country and is even more active in Rome. *J. Cauchi*

CHIGNOLI, V. & FRAENZA, V. La poliomelite nella Provincia di Benevento nel corso dell'anno 1958. Rilievi statistici ed epidemiologici. [**Poliomyelitis in Benevento Province during 1958. Statistical and Epidemiological Findings**] *Acta Med. Italica.* 1959, Jan., v. 14, No. 1, 9–19, 7 figs.

Benevento Province is situated in mountainous and hilly country north-east of Naples, and it has poor road communications: traffic—commercial or tourist—has been limited in the past. The authors have constructed various curves and other graphs to show the incidence and mortality of poliomyelitis in this area during the past 20 years, from figures published by WHO. Up to 1958 incidence rates have been lower than for the rest of Italy and the epidemic season has occurred predominantly in autumn rather than in summer. At about 0·6 per 100,000 the death-rate from the disease is in line with the national figure, but the case-mortality at 18·9% is higher than that of 11·4% reported as average for the rest of the country. Case mortality tends to come down as the incidence rate goes up.

In Benevento, as in other parts of Italy, poliomyelitis has been more prevalent during 1958—100 cases notified and ascertained, giving a rate of 30·2 per 100,000. The death-rate was 3·9 per 100,000 but the case mortality in 1958 was 12%. The majority of patients were under 4 years of age: the number increased steeply in the first 12 months of life, remained at a peak throughout the 2nd year and then dropped in the course of the 3rd year. The provincial centre, with a higher population density, had 23 cases per 100,000 as against 32 per 100,000 in the rest of the province: SABIN in America also noted this inverse relationship between incidence of poliomyelitis and density of population. 65 of the 100 cases occurred in October and November; there was no apparent connexion with either the re-opening of schools or attendance at children's homes. Other parts of the Campania—Naples, Salerno, Caserta—were attacked by the epidemic during July and August and the delay in its spread to Benevento is attributed to the topographical circumstances of this province. The outbreak of virus influenza which hit Naples in the summer of 1957 did not reach Benevento till the autumn. Most years the incidence of poliomyelitis in Benevento Province has shown a small, secondary, rise in the month of January.

There are 77 districts, 15 of which had outbreaks of poliomyelitis in 1958 while 21 others had sporadic cases and 41 had none. 14 of the last have remained free from the disease, at least since as far back as 1936; being "virgin soil" they are likely to suffer severely if the virus were introduced. These 14 districts have 3 factors in common: they are isolated, with poor road communications, at altitudes of 1,000–2,000 ft. above sea-level and have small populations of between 1,800 and 3,000 inhabitants.

The authors have investigated the environmental circumstances—waste disposal, water supply, overcrowding and other housing factors, insect vectors, virus diseases of domestic animals—and failed to find that any of these had a causative relationship to the epidemic; nor did they find any cases resulting from immunization procedures. The infection in various cases, however, was traced to contacts from Naples and other places which had already suffered from the epidemic. The authors believe that human contact is invariably responsible for the spread of the disease. The affected districts in Benevento Province have recently developed increased public transport and more private car traffic and this is taken to have been responsible for the rise of poliomyelitis in 1958. *J. Cauchi*

BROWN, G. C., LENZ, W. R. & AGATE, G. H. **Laboratory Data on the Detroit Poliomyelitis Epidemic—1958.** *J. Amer. Med. Ass.* 1960, Feb. 20, v. 172, No. 8, 807–12.

During the outbreak of poliomyelitis in Michigan in 1958 there were over 1,200 reported cases of paralytic and non-paralytic poliomyelitis, most of them from Detroit, and specimens for virus study were obtained from 1,060 of them. 869 faeces were examined and 191 additional patients were examined serologically. The epidemic was due to both type 1 and 3 poliovirus, a poliovirus being isolated from 218 (177 type 1 and 41 type 3) of 302 paralytic cases, but from only 74 of 567 non-paralytic. No agent was isolated from about 50%

of the non-paralytic cases, and ECHO (97 cases) and Coxsackie (71) viruses were more commonly recovered than polioviruses in this group. 3 patients out of the 302 with paralysis yielded ECHO 9 virus and 2 Coxsackie B5 and serologically 3 additional patients gave evidence of infection with these viruses. 2 paralytic patients appeared to have simultaneous type 1 and 3 virus infection and 2 other patients had during the epidemic successive non-paralytic illnesses due first to type 1 and then type 3 poliovirus. Laboratory-confirmed cases of poliomyelitis predominated in the 0–4-year age-group whereas cases of other aetiology were more evenly distributed between 0 and 14 years of age. The clinical features of cases of non-paralytic disease did not differ significantly according to aetiology. There was a tendency for there to be more cells in the cerebrospinal fluid in cases in which ECHO or Coxsackie viruses had been isolated, than in those in which poliovirus had been isolated.

The incidence of laboratory-confirmed cases of poliomyelitis fell with increasing doses of poliovaccine. Thus for non-paralytic cases it was 21% in unvaccinated, falling to 6% in those given 3 doses of poliovaccine. For paralysed cases the figures were 77% and 29% respectively. A follow-up muscle examination was carried out 60 days from onset in 242 paralysed patients. 187 of these were laboratory-confirmed cases of poliomyelitis. 84% of these patients were still paralysed at 60 days. 83% were unvaccinated and only 4 (2·5%) had had 3 doses of killed poliovaccine. *A. J. Beale*

VANDEPUTTE, M. Endémicité des virus entériques à Léopoldville. [**Endemicity of Enteric Viruses in Léopoldville**] *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 313–18, 2 figs.

"The author has made a study of intestinal viruses in young African children under two years of age in Léopoldville, who showed no clinical signs of any virus disease. The living conditions of these children are characterized by poor hygiene and marked promiscuity. This study, which was spread over an entire year, has revealed: (a) the high endemicity of the enteric viruses in general and of polioviruses in particular in the African's environment; (b) the large number of different strains in circulation and the presence of multiple virus associations; (c) the absence of a well-marked seasonal influence, such as is found in temperate countries.

"During the year of the survey the author was able on two occasions to establish a correlation between clinical manifestations and the data on the spread of viruses collected during this study. He describes, in particular, an epidemic caused by the Coxsackie B2 virus, giving rise to abdominal myalgia, headache and fever, and another caused by a type 3 adenovirus frequently isolated from stools and causing pharyngitis with a high fever, often accompanied by bilateral conjunctivitis.

"He draws attention to the relative harmlessness of the type 3 poliovirus which, although hyperendemic for four months during the survey, did not cause any paralytic case, whereas type 1, which was much less widespread during the same period, was isolated on three occasions from paralysed patients."

(i) SCARBOROUGH, H. **Poliomyelitis: a Danger fo Visitors to Nigeria.** [Correspondence.] *Lance* 1960, Feb. 20, 439. [Also in *Brit. Med. J.*, 196 Feb. 20, 570.]

(ii) MCROBERT, G. R. **Poliomyelitis Risk to Eur peans in the Tropics.** [Correspondence.] *Lance* 1960, Feb. 27, 490. [Also in *Brit. Med. J.*, 196 March, 5, 731.]

i. The author describes a severe case of poliomyelit in a European young man from the north of Nigeria ar comments that this type of disease is "met with not infr quently here, always in Europeans"; treatment in th case was available, a respirator being used, but in othe cases it might well be more difficult. Poliomyelitis almost unknown in adult West Africans, but the la effects are seen in children, and it is probable that infe tion is widespread in early childhood as a result o primitive sanitary and overcrowded living conditions.

The point of this letter is that many Europeans trav to West Africa without having been immunized again poliomyelitis, in ignorance of the risk they run in country saturated with the virus. Immunization can b carried out in Nigeria, but is more difficult there tha in Britain. "It cannot be too strongly emphasized tha prophylactic inoculation against poliomyelitis should b regarded as essential for any European coming to Nigeri even for the briefest of visits."

ii. Sir George McRobert reinforces this by saying tha since the introduction of proguanil the greatest risk fo Europeans anywhere in the tropics is paralytic poliomye litis. Immunization, with subsequent booster doses, ha for some time been provided for members of the Service and other officials, and their families. The improve supply position "enables all who are going to the tropic —even on a short visit—to receive this most necessar inoculation." *Charles Wilcocks*

PAUL, J. R. **The Case for Live Poliovirus Vaccination** *Yale J. Biol. & Med.* 1960, Feb., v. 32, No. 4 241–9. [21 refs.]

In this paper Professor Paul briefly reviews the histor of the development of poliovaccines. The case for attenu ated poliovaccines depends upon the deficiencies of th killed vaccine that it (1) is not 100% effective (perhap 80–90%); (2) requires 3 injections at least and probabl more booster shots to give a long-lasting immunity; (3) i not proving very acceptable, the rate of vaccination bein fairly low even in the U.S.A.; (4) is expensive. Livin poliovaccine is considered on theoretical grounds likel to be superior in giving a long-lasting immunity becaus it mimics the natural infection more closely and appear to prevent, though not completely, reinfection wit virulent viruses. It is recognized that the theoretica advantages for living vaccine remain to be proved an although the method is considered promising it remain in the trial stage. The author strongly advocates a energetic programme for the use of killed poliovaccin while investigating the possible improvements that ma come from the use of attenuated vaccines either in com bination with killed vaccine or by themselves.

A. J. Beale

YOSHIOKA, I. & HORSTMANN, D. M. **Viremia in Infection due to ECHO Virus Type 9.** *New England J. of Med.* 1960, Feb. 4, v. 262, No. 5, 224–8, 3 figs. [14 refs.]

An outbreak of ECHO 9 virus infection in an institution for retarded children was studied. Virtually all the children became infected as judged by virus isolation, or the acquisition of antibodies, and almost all had mild clinical symptoms, usually fever, but 4 had meningitis. Blood was obtained from 15 children up to 5 days before onset of clinical symptoms and 8 had viraemia. In addition, 2 out of 3 asymptomatic children had viraemia. The amount of virus present was low, the highest level being about 174 infectious particles per ml. The suggestion is made that the virus reaches the meninges *via* the blood, viraemia preceding the onset of disease or recovery of virus from other sites. This idea was supported by the results obtained by feeding 2 chimpanzees.

A. J. Beale

PATEL, T. B. & RAO, V. N. **Infectious Hepatitis Outbreak in Bombay City—Epidemiological Investigation Report.** *Indian J. Med. Sci.* 1960, Jan., v. 14, No. 1, 29–37.

An outbreak of infectious hepatitis in January to April 1959 was observed in a high school in Bombay; 7·5% of the 2,000 pupils and 15% of the 60 teachers were affected. A sample survey of the 15,000 population in the district concerned revealed that infectious hepatitis with jaundice had occurred in 5·8% of the population during the same period, and overt typhoid fever in 2·7%; and the water supply showed a high *Escherichia coli* content. The school outbreak was therefore part of an explosive epidemic occurring in this part of the city, and its nature suggested contamination of the water supply. Engineering investigations revealed many broken and corroded water pipes, especially at disused connexions, and where sewage pipes criss-crossed among them; the pressure in the sewage pipes was much higher at times than that in the water pipes, and this also favoured contamination. Recommendations were made for immediate overhaul of the water supplies and for strengthening the hygienic services.

H. Stanley Banks

GALL, E. A. **Posthepatitic, Postnecrotic, and Nutritional Cirrhosis.** *Amer. J. Path.* 1960, Mar., v. 36, No. 3, 241–71, 4 text figs. & 19 figs. on 7 pls. [56 refs.]

ORLANDI, F., MARRI, G., MANUALI, C., MORETTINI, D. & PAVLIDIS, D. **Acute Viral Hepatitis treated with Triamcinolone.** *Panminerva Med.* Turin. 1960, Feb., v. 2, No. 2, 72–3. [Translation from *Minerva Med.*, 1959, v. 50, 2182.]

10 adults suffering from acute viral hepatitis were treated with triamcinolone 0·3 mgm. per kgm. body weight daily. Their progress was estimated by serial liver biopsies, and frequent estimations of serum bilirubin and transaminases along with alkaline phosphatase and serum flocculation tests. A sharp fall in serum bilirubin and transaminases was noted and improvement in histopathological findings: flocculation tests showed less change. The authors feel that, on the basis of their previous experience with this disease, the drug was effective in doses smaller than required with other steroids but that it sometimes fails: its action seemed to be due to modification of the basic disease process.

A. B. Christie

MILES, J. A. R. **Epidemiology of the Arthropod-Borne Encephalitides.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 339–71. [Numerous refs.]

This is a detailed concentrated review of the epidemiology of those arborviruses which cause encephalitis in man. Each is considered in turn: its distribution, epidemics and transmission (the vectors are tabulated). The relationships between vectors and vertebrate hosts are discussed with particular reference to the American equine encephalitides, Japanese encephalitis and Murray Valley encephalitis. The problems of inter-epidemic survival of viruses and the factors concerned in starting epidemics are then discussed. Control of these infections depends on attempts to control the vectors, vaccination where possible, sometimes on passive immunization of individuals, and on the careful ecological study of undeveloped areas before they are closely settled. The difficulties in interpretation of serological findings within the closely related groups of arborviruses are finally discussed. [This is a valuable review for the general reader and is a most valuable source of references.]

C. E. Gordon Smith

SHOPE, R. E. & ANDERSON, S. G. **The Virus Aetiology of Epidemic Exanthem and Polyarthritis.** *Med. J. Australia.* 1960, Jan. 30, v. 1, No. 5, 156–8. [17 refs.]

An epidemic of exanthem and polyarthritis involving over 1,000 persons occurred in the Murray Valley in South Australia in April–May 1956 [this *Bulletin*, 1958, v. 33, 16, *ter*]. The rash which often covered the whole body started as discrete macules, became papular and sometimes vesicular. Joint pains, mainly in the small joints of the extremities, usually preceded the rash—swelling was however rare. Joints symptoms lasted from 2 days to 8 months. Fever seldom occurred and the highest recorded was 100·8°F. Tender lymphadenopathy and disturbances of superficial sensation occurred in some patients. Leucocyte counts varied from 2,800–7,000 per cmm. The incubation period was estimated at 10–11 days. Similar epidemics have been recorded in Australia and the south-west Pacific and these are tabulated [see, for example, *ibid.*, 1945, v. 20, 260; *Trop. Dis. Bull.*, 1946, v. 43, 786; 1947, v. 44, 206].

16 pairs of acute and convalescent sera from patients in this outbreak were tested for haemagglutinin-inhibiting antibody to group A arboviruses (Chikungunya, Semliki Forest, Mayaro, Middelburg, Venezuelan, western

and eastern equine encephalitides, Sindbis, and 2 from culicine mosquitoes in Malaya—AMM 2021 and AMM 2354). 6 serum pairs had significant rises in antibody to 1 or more of these viruses. Both of 2 pairs tested in a complement-fixation test showed increases in titre against AMM 2021, but not against the 9 other viruses. In intraperitoneal neutralization tests against about 100 LD50 of AMM 2021 and AMM 2354, 4 of 6 pairs changed from negative to positive against one or other or both. The epidemic thus appears to have been due to a group A arborvirus, perhaps one not yet isolated.

17 of 24 human sera from healthy people in New Guinea and north-east Australia had haemagglutinin-inhibiting antibody to group A viruses and 6 of 8 Australian sera neutralized AMM 2021 virus. Little evidence of antibody was found in 26 human sera from Bougainville Island or in sera from 7 water-rats and 18 chickens from the Murray Valley shortly after the epidemic. Group A arboviruses (or arborvirus) appear to be endemic in New Guinea and north-east Australia.

C. E. Gordon Smith

KARSTAD, L., VADLAMUDI, S., HANSON, R. P., TRAINER, D. O., Jr. & LEE, V. H. **Eastern Equine Encephalitis Studies in Wisconsin.** *J. Infect. Dis.* 1960, Jan.–Feb., v. 106, No. 1, 53–9, 1 fig. [11 refs.]

Sera, and blood samples on filter-paper, were collected from wild and domestic animals in Wisconsin in 1957–58 and tested for neutralizing antibodies against eastern equine encephalitis virus. The sera and antibiotic-treated filter-paper extracts were not inactivated and the neutralization tests were made in the allantoic cavity of 9–10-day chick embryos. Blood on filter paper was collected from pheasants and grouse killed on the roads and from pheasants shot by hunters. Eastern equine virus was isolated from 1 of 6 of pheasants' bloods dried on filter-paper tested after 16 days' storage at room temperature but not from 93 tested after 22 or more days' storage. The strain isolated caused a more prolonged illness in mice than the stock strain. Experimentally chicken blood with a virus titre of $10^{7.3}$ LD50 dried on filter paper had a titre of $10^{5.2}$ after 3 days' and $10^{1.8}$ after 12 days' storage at room temperature. Virus could not be demonstrated on the 21st day.

1 of 5 horses which had had encephalitis had eastern equine antibody and 1 of the others western equine antibody. 3 of 12 pigs had eastern equine antibdy. 11 of 16 squirrels (both tree and ground species) had antibody. 45 of 89 pheasants (*Phasianus colchicus*), mostly killed on the roads in winter, and 26 of 52 ruffed grouse (*Bonasa umbellus*) had antibody, as did 4 of 10 quail and smaller numbers of 6 other non-game birds. Antibody was found in 1 of 3 black duck (*Anas rubripes*) —the first record of antibody in a duck.

100 farm-reared pheasants were released in the field in mid-September and 19 were shot 33 days later: only 1 of these had significant antibody before release but all except 1 had antibody 33 days later, suggesting that they had been naturally infected during this period. [The table of "19 paired sera" in fact contains only 12—this is unexplained.] This also suggests that the arthropod-borne infection of pheasants causes a much milder disease than the severe form with high mortality which is transmitted by pecking in penned birds.

C. E. Gordon Smith

WALLIS, R. C., TAYLOR, R. M. & HENDERSON, J. F. **Isolation of Eastern Equine Encephalomyelitis Virus from *Aedes vexans* in Connecticut.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 442–4. [13 refs.]

"The virus of eastern equine encephalomyelitis was isolated from one pool of mosquitoes limited to 13 specimens of *Aedes vexans* collected Sept. 1, 1959, at Farmington, Conn. Distribution, seasonal incidence and bionomics of this mosquito fit epidemiological qualifications necessary for implication as a vector of eastern equine encephalomyelitis in this area."

BENNINGTON, E. E. & SHERMAN, Ida L. **A Note on Reported Cases of Encephalitis and Soil Temperatures in Colorado.** *Mosquito News.* 1960, Mar., v. 20, No. 1, 34–8, 3 figs.

The soil temperature inversion date is when the temperature of the surface soil changes from colder than to warmer than, the subsoil. In the Colorado area *Culex tarsalis*, the encephalitis virus vector, emerges from hibernation immediately after the inversion date. There may be 2 or rarely 3 inversions in a single spring due to returns to winter soil conditions. The inversion dates from 1942 to 1957 in N.E. Colorado were compared with the numbers of cases of human encephalitis in the area in each year—a tendency was found for larger numbers of encephalitis cases in years with late inversion dates. A similar tendency was seen in the incidence of encephalitis in equines. This suggests that a short *C. tarsalis* season may lead to more virus dissemination than a long one. There is an interval of about 2 months between the inversion date and the onset of encephalitis cases.

C. E. Gordon Smith

BAQUERIZO AMADOR, L. & MÁRMOL, C., Fanny. Aislamiento del virus de la encefalomielitis equina tipo venezolano del suero sanguíneo y faringe de un caso humano. [**Isolation of Equine Encephalomyelitis Virus Venezuelan Type from the Serum and Pharynx of a Patient**] *Rev. Equatoriana de Hig. y Med. Trop.* Guayaquil. 1959, Jan.–Mar., v. 16, No. 1, 1–8.

The English summary appended to the paper is as follows:—

"One of our technicians inoculated herself by accident with equine encephalitis virus, Venezuelan type, by puncturing her finger with a hypodermic needle she was using to inoculate mice.

"She became ill 24 hours after the accident with headache, lassitude and fever with chills. The disease was short and the patient came to work seven days after the

onset. The patient did not show nervous symptoms or sequelae.

"During the acute phase of the illness the virus was recovered from the blood and the pharynx of the patient. A known Venezuelan antiserum neutralized both blood and pharyngeal strains.

"The patient's serum showed very high antibody titer against the virus isolated from the patient and against a known Venezuelan strain."

MISHIN, A. V. & GERASIMOVA, E. N. **[Epidemiological Characteristics of Tick-Borne Encephalitis in the Udmurt Autonomous Soviet Republic]** *Med. Parasit. & Parasitic Dis.* Moscow. 1959, v. 28, No. 2, 137–42, 1 map. [In Russian.] English summary.

The incidence of tick-borne encephalitis in the Udmurt Autonomous Republic is among the highest in the Soviet Union; between 1954 and 1957 the annual number of notified cases ranged from 435 to 848, a mean incidence of 6·65 per 10,000. The disease was mainly localized to 4 of the 29 regions of the Republic, in which 76·8% of the total number of cases occurred. Cases occurred each year from May to August. Investigations carried out in the field in 1956 and 1957 showed that the incidence of the disease lagged behind the extent of activity of ticks; the high incidence in July and August therefore occurred at a time when the activity of the ticks was low, and was attributed to the increased activity of the population in the woods and meadows at this time. The main age incidence was seen in the 21–29-year age-group (25·1% of all cases), and the main occupational incidence was among collective farm workers (28·7%); 82·7% of cases were attributed to bites from the tick *Ixodes ricinus* and 17·3% to the consumption of infected goat's milk. In an analysis of 1,803 cases a biphasic course was observed in 48·8%; in 588 cases the mean duration of the first febrile period was 6·87 days and of the second 7·26 days.

D. J. Bauer

LVOV, D. K. **[An Immunological Population Study within a Reservoir of Tick-Borne Encephalitis in a Piedmont Forest Area of the Krasnoyarsk Region]** *Med. Parasit. & Parasitic Dis.* Moscow. 1959, v. 28, No. 2, 143–9, 1 chart. [Numerous refs.] [In Russian.] English summary.

A serological investigation has been carried out on the native population of an area in the Krasnoyarsk district affected by tick-borne encephalitis, consisting of foothills intersected by deep ravines and covered by dwarf coniferous vegetation. Neutralizing antibody to tick-borne encephalitis virus was present in 78 of 262 (30%) and complement-fixing antibody in 43 of 214 (20%) persons examined. The incidence of neutralizing antibody increased with time of residence in the district, being 14·6% in persons resident for 1–3 years and 48% in persons resident for 21–30 years, and a consideration of the values of the neutralization index in these persons in comparison with a group of immune persons not exposed to natural infection indicated that the antibody titre was maintained at a high level by repeated subclinical infections.

D. J. Bauer

JANDÁSEK, L., with the technical assistance of Marie SVOBODOVÁ. Einfluss des Thyroxins auf die experimentelle Zeckenenzephalitis der infantilen Ratte. **[The Influence of Thyroxin on the Course of Experimental Tick Encephalitis of Young Rats]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Apr., v. 119, No. 4, 365–9.

The English summary appended to the paper is as follows:—

"Suckling rats were treated subcutaneously from the second day of life with 0·1 mg. thyroxin per day. At the 11th day they were infected with 10^5 DL50 tick encephalitis virus, strain Hypr. The thyroxin treated animals showed shorter survival times than the controls. Neither the antibody production nor the number of virus carriers were influenced by thyroxin."

DE CHENAR, C. **On the Pathogenesis of Neuronal Lesions in Viral Encephalomyelitides.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 1, 1–17. [23 refs.]

ENDERS, J. F., MCCARTHY, K., MITUS, Anna & CHEATHAM, W. J. **Isolation of Measles Virus at Autopsy in Cases of Giant-Cell Pneumonia without Rash.** *New England J. of Med.* 1959, Oct. 29, v. 261, No. 18, 875–81, 4 figs. [26 refs.]

3 fatal cases of giant-cell pneumonia are described, occurring in children aged 3, 4 and 2 years who were respectively suffering from mucoviscidosis, leukaemia and Letterer-Siwe disease. There was definite or probable exposure to measles in each case, but none of the patients showed any clinical manifestations of the disease. The diagnosis of giant-cell pneumonia was established at autopsy by histological examination. Infective agents producing syncytia or giant cells were isolated after death in primary monolayer cultures of human kidney cells from mucopurulent material obtained from the bronchi in case 1, from the lung in case 2 and from the liver and lung in case 3. In stained preparations of infected cultures eosinophilic intranuclear and intracytoplasmic inclusion bodies were seen, resembling those characteristic of measles virus. The agents would not grow in human amnion cells at first, but could be adapted after 6–8 passages in kidney cells; the same cytopathic effect was also produced in monkey kidney and HeLa cells. 2 of 3 cynomolgus monkeys infected intravenously, intranasally and intramuscularly with culture fluid of the 2nd and 3rd passages developed viraemia between the 5th and 9th days after infection, and all 3 animals developed neutralizing and complement-fixing antibodies in high titres to both measles virus and the giant cell pneumonia agents. No rash or other signs of measles infection was observed. The results indicate that measles virus is responsible for the causation of giant-cell pneumonia.

D. J. Bauer

MITUS, Anna, ENDERS, J. F., CRAIG, J. M. & HOLLOWAY, Ann. **Persistence of Measles Virus and Depression of Antibody Formation in Patients with Giant-Cell Pneumonia after Measles.** *New England J. of Med.* 1959, Oct. 29, v. 261, No. 18, 882–9, 1 fig.

The authors have observed 4 cases in which children suffering from leukaemia developed measles complicated by severe pneumonitis. The ages of the patients ranged from 2¾ years to 3 years and 11 months; they developed measles during a remission in the course of acute leukaemia. Pneumonitis supervened and led to death in 2 cases, and giant-cell pneumonia was found at autopsy. A presumptive diagnosis of this condition was also made in the 2 patients who recovered. Measles virus was isolated in human kidney cell cultures from throat washings, lung or liver tissue of 3 patients, and could subsequently be adapted to passage in human amnion cells. Titration of lung material showed that it contained measules virus in a titre of between 100 and 1,000 ID50 per gm. The strains of virus isolated were identified from their cytopathic effect and from the results of neutralization and complement-fixation tests with measles reference antisera. In 2 patients who died the virus could still be found in the respiratory tract 22 days and 1 month after the onset of the rash, and antibodies failed to appear or were only present in low titres. A similar depression of the immune response was also seen in the 2 patients who recovered. *D. J. Bauer*

FERGUSON, A. W. **Rubella as a Cause of Thrombocytopenic Purpura.** *Pediatrics.* Springfield, Ill. 1960, Mar., v. 25, No. 3, Pt. 1, 400–408. [38 refs.]

"Case histories are presented of two children in whom thrombocytopenic purpura followed rubella, and a third case is described in which purpura may have been secondary to a modified rubella infection. The serum of two of the children appeared to contain platelet agglutinins. The clinical features of these 2 and 17 other published cases of post-rubella purpura are summarized and discussed.

"Some clinical and pathologic aspects of acute thrombocytopenic purpura in childhood are discussed, and it is suggested that infections mild enough to pass unrecognized, such as rubella, may precipitate the disease more frequently than is suspected."

BLANC, G. & ASCIONE, L. Rôle de certains arthropodes piqueurs dans la conservation et la transmission du virus de la chorioméningite lymphocytaire. [**Role of Certain Biting Arthropods on the Maintenance and Transmission of Lymphocytic Choriomeningitis Virus**] *Bull. Acad. Nat. Méd.* 1960, Mar., v. 144, Nos. 9/10, 177–9.

Larval *Amblyomma variegatum* were fed on a rabbit which had received an intravenous inoculation of 4 ml. of blood from a guineapig in the febrile stage of lymphocytic choriomeningitis. The rabbit blood 20 minutes after inoculation was infective to guineapigs by intraperitoneal inoculation. The ticks fed for 6–7 days. The larval and nymphal ticks were found to be infected a were nymphs derived from the infected larvae and adult from infected nymphs. Transmission by tick bite wa achieved and the excreta of infected ticks were infectec [No details are given of the experiments with the fe larvae and nymphs and a proper evaluation of this wor is therefore impossible.] *C. E. Gordon Smith*

GREEN, N. & GOLDENBERG, H. **Acute Hemolyti Anemia and Hemoglobinuria complicating Infec tious Mononucleosis.** *Arch. Intern. Med.* 196(Jan., v. 105, No. 1, 108–11. [24 refs.]

This is a well documented article describing a case c acute haemolytic anaemia complicating infectious monc nucleosis and giving a good account of the literatur especially that dealing with the presence of auto-immun antibodies in this disease. Of the 21 cases found in th literature only in 6 have haemolytic antibodies actuall been demonstrated. In other cases hypersplenism secor dary to the splenomegaly found in a minority of case of infectious mononucleosis may have been the cause o the haemolytic anaemia, but in such cases the presenc of a possible auto-immune mechanism was not adequatel investigated.

The patient was a man of 45 who, on the 11th day c febrile symptoms, suddenly passed red urine resemblin venous blood, but containing few red cells. His serur was also red, and his haemoglobin value dropped suc denly from 68% to 31%. His peripheral blood containe numerous abnormal monocytes, and the heterophil agglu tination titre, after differential absorption, was 1:320 The direct Coombs antiglobulin test was positive, an cold agglutinins were present in a titre of 1:256, bu haemolysins could not be detected. Treatment was b packed red cells 1,000 cc. daily along with prednisone o cortisone for 4 days; this produced little improvement i the urine and his haemoglobin remained very low (35% The medication was then changed to corticotrophin 2 units daily in continuous intravenous drip, and afte this (not necessarily because of it) the urine began to clea and recovery to set in.

The aetiology of this case was considered to be on a auto-immune basis. *H. Stanley Banks*

ROSALKI, S. B., JONES, T. G. & VERNEY, A. F **Transaminase and Liver-Function Studies i Infectious Mononucleosis.** *Brit. Med. J.* 196(Mar. 26, 929–32. [24 refs.]

Liver involvement in glandular fever is not ofte apparent clinically, though liver function tests are ofte abnormal; but since many of these reflect changes i serum proteins, they may denote antibody productio rather than hepatic damage. An investigation of 1 patients with glandular fever at the Westminster Hospital London, was made to determine whether cytotoxic live changes could be revealed by a rise in the serum conten of the transaminases, glutamic-oxaloacetic and glutamic pyruvic (SGOT and SGPT).

Of the 19 patients, only 1 was clinically jaundiced, an 4 had palpable livers. 18 patients showed an elevatio

of the serum transaminases, and 12 patients tested within 7 days of the onset all showed this feature. The rise in SGOT ran roughly parallel with that of SGPT, and the raised levels usually reverted to normal by the 5th week. The transaminases were elevated in 2 of the 4 patients (acceptable on other grounds) in whom no heterophil antibody could be demonstrated. The transaminase rise in glandular fever differed from that in infective hepatitis in that in the former it hardly ever exceeded 500 units/ml., and did not reach its peak until the second week of illness. Normal levels were found in the following controls: upper respiratory infections (10 cases), lymphosarcoma (3), Hodgkin's disease (2).

Conventional liver function tests in this series of patients were less often abnormal, and were not affected as early as the transaminase increase. The latter, appearing in the first week, is therefore of some diagnostic value. Its constancy suggests that it is worth taking care, in all cases of glandular fever, to reduce the chance of permanent liver damage by rest, low fat and high protein and carbohydrate diet, with parenteral fluids if there is anorexia. Finally the suggestion is made that if hepatotoxic effects are so constant, the infective agent may commonly pass into the faeces, rendering them infective.

Alan B. Raper

SMITH, R. E. & DARLING, R. M. **Encephalopathy of Cat-Scratch Disease.** *J. Dis. Children.* Chicago. 1960, Jan., v. 99, No. 1, 107–8.

In this paper there is a short account of the history of cat-scratch disease which, though first described in 1932, was not formally recognized as an entity till 1950. Its complications which are mentioned have been rare and of these involvement of the nervous system has been reported in only 14 cases [this *Bulletin*, 1952, v. 27, 1110; 1953, v. 28, 24; 1954, v. 29, 812; 1957, v. 32, 1048].

A detailed case report of the disease and its diagnosis in a boy aged 11 years is given here. The boy was admitted to hospital because of a convulsion. 3 weeks previously he had had fever of 102°F. with severe cough and also complained of a tender mass in the right axilla. There was also an abrasion on the right hand caused by a pet cat. After admission he had severe headache, tremors, convulsions and developed a stuporous state. There were some changes in the nervous system on testing of the reflexes. He improved gradually and by the third day was alert and well orientated. Follow-up examination showed that he had recovered completely and had no neurological sequelae.

M. E. Delafield

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

SKERMAN, V. B. D. **A Guide to the Identification of the Genera of Bacteria with Methods and Digests of Generic Characteristics based on Data given in the Seventh Edition of Bergey's Manual of Determinative Bacteriology and on Original Papers.** pp. ix + 217, illustrated. 1959. Baltimore 2: The Williams & Wilkins Co., Md., U.S.A. London: Baillière, Tindall & Cox, Ltd., 7 & 8, Henrietta Street, W.C.2. [44s.]

In 1949 Skerman first published his mechanical key for the generic identification of bacteria. This was criticized [this *Bulletin*, 1950, v. 25, 168] mainly on the grounds that it might give theoretically possible but practically absurd results. Skerman modified his scheme and in a greatly improved form it appeared in the seventh edition of *Bergey's Manual of Determinative Bacteriology* [*Ibid*, 1958, v. 33, 421]. The book under review consists of (1) a reprint (with a few additions and further improvements) of the mechanical key from Bergey's *Manual*, (2) definitions of genera and notes on how the species within them are distinguished, and (3) brief descriptions of media and methods used in carrying out these distinguishing tests.

Criticism levelled at the early stages of development of this mechanical key are not applicable to the present version, which the reviewer has used successfully and recommended to others since its appearance in Bergey's *Manual*. Page references are made to genera as named and defined in the *Manual* (7th edition), and also, where applicable, to the corresponding genera in *Topley and Wilson's Principles of Bacteriology and Immunity* (4th edition), [*Ibid*, 1956, v. 31, 687].

The key is up-to-date and includes references to groups defined by the International Enterobacteriaceae Subcommittee in its 1958 report, and to genera such as *Leptotrichia, Mima, Jensenia, Aerococcus,* and *Waksmania,* and a series of organisms, the Krassilnikoviae, which are not described in the two bigger reference books.

After tracking down an unknown organism in the key, the generic diagnosis can be confirmed by reference to the descriptions given in the second section of the book,

and this section may suggest additional tests that need to be done. The third section describes methods (some original) for carrying out many of these tests. In writing a book of this kind it must be difficult to know what to leave out and what to include, but omissions that should be rectified in a subsequent edition concern the coagulase test (in which the errors possible through using citrated plasma might be indicated), tests for fibrinolysins, lecithinases, hydrolysis of aesculin and sodium hippurate, and the deamination of phenylalanine, to mention a few that are regularly used by medical bacteriologists.

This book can be strongly recommended, more especially to those who have to identify bacteria from unfamiliar sources and to the beginner in bacteriology. It is an essential reference book for any diagnostic laboratory.

S. T. Cowan

VAN ITERSON, Woutera & RUYS, A. Charlotte, with the technical assistance of S. V. LUNEL-FOKKEMA. **On the Nature of P.P.L.O. II. Electron Microscopy.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 1, 9–22, 14 figs. [15 refs.]

"Colonies of the three species of *Mycoplasma* of human origin were frequently found to contain coccoid elements. From electron micrographs it is deduced that the principle component of P.P.L.O. colonies are vesicular units of variable sizes. Usually these vesicular elements are largely vacuolar in nature. They then contrast strongly with the compact cocci. This study gives a number of data which seem to suggest that the coccoid elements and the P.P.L.O. forms belong together. Since the cocci are of definite bacterial structure the *Mycoplasma* species of human origin might represent the L phase variant of minute coccoid bacteria."

KAFFKA, A. & WALTHER, J. Bakteriell bedingte Injektionszwischenfälle. [**Accidents during Courses of Injections, caused by Bacterial Contamination**] *Zent f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 632–40. [14 refs.]

As a sequel to one of a series of intravenous injections of a mixture of 10% laevulose and liver autolysate which were being given to patients with cirrhosis, there were deaths with internal haemmorhages and in the 3 other patients a very sharp reaction starting within 30 minutes which took the form of rigors, pains in head and back high fever, bilirubinaemia and marked increase in the transaminase of the plasma.

A very full investigation of the residual solution in the reservoirs from which the materials had been taken was carried out and resulted in the following findings:—

The liver autolysate was sterile but the laevulose solution was turbid with some brownish discoloration and yielded a culture of a Gram-negative bacterium with a limited range of suitable growth temperature 22°–30°C. straight, with 1 or occasionally 2 monopolar flagellae these were classified with the Pseudomonadaceae but not placed more exactly.

It was established experimentally that this bacterium would grow readily in 10% laevulose solution and traces of liver autolysate and that such cultures were markedly pyrogenic in rabbits. It was also shown that they were agglutinated in high concentrations of human serum.

A close investigation of the technique adopted in handling and administering these injections revealed the following facts:— both ingredients of the injection were prepared in rubber-capped ampoules, sterile cannulae were introduced to these and then a series of syringes were filled from them, 5 ml. of liver, autolysate being drawn first with a 20 ml. syringe and then 15 ml. of 10% laevulose. The partial vacuum produced by the withdrawal in the laevulose bottle would inevitably cause a slight contamination of that solution with liver autolysate and with bacteria from the air. The contents of the bottles were normally used up one at a time but on the occasion in question the material had remained at room temperature for 2 days after a withdrawal and the remainder had then been used.

[The possibility of catastrophes of this kind is, of course, obvious to any one in the habit of doing experimental bacteriological work but probably less so to many who handle patients and are accustomed to use solutions or suspensions prepared in bulk in rubber-capped containers, hence this review at some length.]

J. W. McLeod

See also p. 651, ANGUS, **The Effects of Mechanical Ventilation on Airborne Bacteria.**

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection**

BRITISH MED. BULL. 1960, Jan., v. 16, No. 1, 1–85, illustrated. [Numerous refs.] **Antibiotics in Medicine.**

L. P. GARROD (pp. 1–2), introducing this symposium, comments that progress has been so rapid that textbooks on antibiotics are likely to be out of date before they are printed. The symposium is intended to fill this gap by presenting enough current information, much of which can otherwise be found only in original papers, to cover the most important facts about antibiotics and to allow the reader to form his own opinions on the more controversial aspects of the subject. [The papers which follow succeed admirably in fulfilling these aims.

and the volume as a whole should serve as a useful and thoroughly up-to-date textbook of antibiotics for the general medical reader.]

E. P. Abraham and G. G. F. Newton (*Chemistry and Classification of Antibiotics*, pp. 3–10) recognize 3 main chemical groups of antibiotics. Those which can be derived from amino acids include penicillin, chloramphenicol, bacitracin, polymyxin and cycloserine. The group derivable from acetate includes the tetracyclines, griseofulvin, the erythromycin group which consist of lactone rings called macrolides, and the 2 conjugated polyenes, amphotericin B and nystatin. The third group, derivable from sugars, contains streptomycin, kanamycin and neomycin. Novobiocin, vancomycin and ristocetin are meantime relegated to a miscellaneous group. Full structural formulae are given for most of these antibiotics.

E. F. Gale (*The Nature of the Selective Toxicity of Antibiotics*, pp. 11–15) discusses the mode of action of penicillin, polymyxin, and chloramphenicol. Most is known about penicillin which appears to interrupt the synthesis of cell-wall substances. The damaged or incomplete cell wall ceases to protect the contained protoplast which is lysed by osmotic action. Polymyxin probably acts on the cell membrane which then allows the escape of metabolites essential to the organism. Chloramphenicol appears to interfere with the synthesis of bacterial protein.

M. R. Pollock (*Drug Resistance and Mechanisms for its Development*, pp. 16–22) considers mechanisms of drug resistance such as metabolic pathways of the organism which are insusceptible to the drug, failure of the antibiotic to penetrate the bacterial body, and destruction of the drug before it reaches the bacterium. The acquisition of resistance by an individual bacterial cell may be due to the antibiotic inducing enzymic changes which are not heritable by the cell's progeny, or by gene mutation or recombination which are not influenced by the drug. Adequate evidence is not yet available that genetic changes causing resistance have actually been induced by an antibiotic.

L. P. Garrod and E. F. Scowen (*The Principles of Therapeutic Use of Antibiotic*, pp. 23–28) discuss the points to be considered in choosing an antibiotic. These include the usual antibiotic sensitivity of the organism, the chances of resistance developing and of toxicity with different antibiotics, and the appropriate route of administration which depends on the absorption of the drug from the gut and the diffusion into body cavities or cerebrospinal fluid. A table sets out the minimal inhibitory concentration of all the principal antibiotics for most important pathogens. The duration of treatment, the indications for laboratory investigations, and minor points, such as the optimal *p*H of urine in treating urinary infections, are fully considered.

J. C. Gould (*The Laboratory Control of Antibiotic Therapy*, pp. 29–34) describes *in-vitro* testing of antibiotic sensitivity by serial-dilution methods in fluid and on solid media, and by the more frequently employed agar-diffusion technique. He considers that an agar-diffusion test done with the original specimen as inoculum gives a truer estimate of sensitivity than a test of a single colony in subculture. The problems of testing sensitivity to antibiotic combinations and the correlation of *in vitro* findings with clinical response are discussed.

J. M. Robson and G. A. H. Buttle (*The Pharmacology of Antibiotics*, pp. 35–41) summarize the important information on preparations, administration, absorption, diffusion and excretion of all the antibiotics in use in Britain, including such recently introduced drugs as cycloserine, kanamycin, vancomycin, amphotericin B, and griseofulvin. The urinary excretion and penetration into cerebrospinal fluid, bile and serous cavities of the more common antibiotics are given in tabular form.

B. W. Lacey (*The Rationale and Management of Combined Therapy*, pp. 42–46) states the case for using combinations of antibiotics to increase the effectiveness of therapy as with streptomycin and a tetracycline in brucellosis, to cover all likely pathogens as in an undiagnosed purulent meningitis, to prolong effective therapy as in tuberculosis, and to prevent superinfection. Combined therapy would be of general value in suppressing the emergence of resistant tubercle bacilli and staphylococci. Commercial fixed-dose mixtures should be avoided.

E. G. L. Bywaters (*Preventive Use of Antibiotics in Medicine*, pp. 47–50) states that antibiotic prophylaxis has succeeded in protecting against infection during meningococcal epidemics, in reducing exacerbations of chronic bronchitis, in preventing endocarditis after dental extractions in patients with abnormal heart valves, and in preventing recurrences of rheumatic fever. It has failed to reduce secondary infection in measles, in comatose patients, and in respiratory poliomyelitis. Penicillin prophylaxis of streptococcal infections to prevent rheumatic fever has only one drawback, that of sensitization of the patient to penicillin.

G. W. Taylor (*Preventive Use of Antibiotics in Surgery*, pp. 51–54) advises against antibiotic prophylaxis in clean surgical procedures. Penicillin should be given systemically to prevent anaerobic infections after severe injuries and to prevent infection after oral and oesophageal surgery, and locally to prevent streptococcal infection of burns. Sulphonamide or neomycin by mouth is advisable before operations on the colon, but gastric or small-bowel operations need no antibiotic prophylaxis. Topical application of bacitracin may prevent infection after lengthy brain operations.

J. Crofton (*The Chemotherapy of Tuberculosis*, pp. 55–60) considers that patients whose tubercle bacilli are fully sensitive will almost always be cured by prolonged treatment with a combination of 2 of the 3 drugs, streptomycin, PAS and isoniazid. The less powerful drugs, viomycin, tetracycline, pyrazinamide, cycloserine, and "1314", are discussed and full details are given of their use in treating patients whose organisms are resistant to one or more of the 3 main antituberculous drugs.

A. E. Dormer (*Treatment of Bacterial Endocarditis*, pp. 61–66) considers that penicillin is still the mainstay of treatment of endocarditis. The additional use of streptomycin shortens the duration of therapy in *Streptococcus viridans* cases and is essential in treating *Strep. faecalis* infections. The wide variety of drugs and their combinations in staphylococcal cases, and the promising results reported with ristocetin and vancomycin against various organisms, are discussed.

D. M. Dunlop and J. M. Murdoch (*The Dangers of Antibiotic Treatment,* pp. 67–72) describe in detail the incidence and importance of hypersensitivity and Jarisch-Herxheimer reactions, local irritation, systemic toxicity, and consequent superinfection following the use of all the antibiotics at present in common use.

E. J. L. Lowbury (*Clinical Problems of Drug-resistant Pathogens, pp.* 73–78) discusses the increase in proportion of antibiotic-resistant staphylococci, and the increase in staphylococcal surgical wound infections and infections of mothers and babies in maternity hispitals in recent years. The increase in resistant strains of salmonellae, shigellae and enteropathogenic *Escherichia coli,* and of various Gram-negative bacilli which infect wounds and the urinary tract, is also considered.

R. Cruickshank (*Laboratory Uses of Antibiotics,* pp. 79–81) mentions 4 laboratory techniques which make use of antibiotics. Antibiotic-containing selective culture media are of value as Bordet-Gengou medium with penicillin and neomycin-Nagler plates for cultivating *Clostridium welchii.* Antibiotic-sensitivity patterns offer a rough but simple method of typing staphylococci. The addition of antibiotics makes possible the isolation of viruses in tissue culture, eggs, and animals from specimens containing bacteria. Finally antibiotics have proved a helpful tool in studies of bacterial growth and variation.

A. H. Campbell (*The Search for New Antibiotics,* pp. 82–85) describes the isolation of antibiotics by screening streptomycetes for antibacterial products, checking by chromatography if the new antibiotic is the same as known antibiotics, testing it for cross-resistance with other antibiotics, and for animal toxicity. These standard methods may miss useful antibiotics as with griseofulvin, the value of which was not realized until 20 years after its isolation. *I. B. R. Duncan*

Bacharach, A. L., Clark, Barbara J., McCulloch, Marian & Tomich, E. G. **Comparative Toxicity Studies on Ten Antibiotics in Current Use.** *J. Pharmacy & Pharmacol.* London. 1959, Dec., v. 11, No. 12, 737–41.

These authors re-examined the comparative toxicity of 10 important antibiotics because published findings are not in fact comparable. The LD50 by 4 routes, intravenous, intraperitoneal, subcutaneous and oral, was determined in 2 strains of mice. By the intravenous route the order of increasing toxicity was penicillin < bacitracin < chloramphenicol < oxytetracycline < tetracycline < erythromycin < chlortetracycline < streptomycin < neomycin < polymyxin. Neutralization of the (acid) solution of tetracycline hydrochloride diminished its subcutaneous but increased its intravenous toxicity. Some differences in relative toxicity by different routes, and minor differences in susceptibility between strains of mouse and sexes, are noted. Strain differences in susceptibility to drugs are briefly discussed, and it is emphasized that in reporting such findings the strain of animal used should be specified.

L. P. Garrod

Snell, Neva S. & Lewis, J. C. **Errors caused b Stainless-Steel Cylinders in Plate Bioassay** *Antibiotics & Chemotherapy.* New York. 195 Oct., v. 9, No. 10, 609–12.

Suspecting that stainless steel cylinders were causin loss of activity in antibiotic solutions placed in them fo assay, these authors submerged 25 cylinders in 10 ml. solutions for 24 hours, and then assayed the solutio Both bright and tarnished cylinders were teste Chloramphenicol and streptomycin were unaffected, b losses of activity of up to 80% were observed in tes with penicillin, chlortetracycline, bacitracin, subtilin an aterrimin (the 2 latter being antibiotics under study whe this effect was first suspected). Tarnished cylinders ha more effect than bright; this was confirmed by simp direct assays using both. There was a greater percentag loss in a weak than in a more concentrated solution, an the result was affected (not always in the same directio by the degree of purity of the antibiotic.

L. P. Garrod

Garrod, L. P. **Relative Antibacterial Activity o Three Penicillins.** *Brit. Med. J.* 1960, Feb. 2 527–9.

The activities of penicillin G and penicillin V again staphylococci, streptococci, *haemophilus* and *prote* were compared with that of 6–(alpha-phenoxypropiona mido) penicillanic acid, an antibiotic commercially know as Broxil and referred to in this paper as penicillin I The minimum inhibitory concentration (MIC) of eac of the 3 penicillins for 36 penicillin-sensitive strains an 38 penicillin-resistant strains of *Staphylococcus pyogene* 11 strains each of *Streptococcus pyogenes* and *St faecilis,* 12 strains of pneumococci, 7 strains of *Haemo philus influenzae,* and 10 strains of *Proteus mirabili* were determined by a plate-dilution method with a sma inoculum. The penicillin-resistant staphylococci wer also tested by a tube-dilution method with a heav inoculum. In this method the MIC depends on th amount of penicillinase produced by the organism.

All 3 penicillins gave almost the same MIC with eac of the penicillin-sensitive staphylococci. Similar result were found by the plate method with the penicillin-re sistant staphylococci but the tube method with a heav inoculum showed major differences in the sensitivity o these strains to the 3 penicillins. All the resistant strain were more sensitive to V or B than to G, the difference being in some cases 256–fold, and most were more sen sitive to B than to V. There was little difference in th sensitivities of the streptococci to the 3 penicillins. Peni cillin G was much more active against *H. influenzae* tha B and V, which were very similar to each other i activity. Against *Pr. mirabilis,* G was considerably th most active, and V was more active than B.

The author concludes that B is the penicillin of choic for the treatment of resistant staphylococcal infections and he makes the point that it may become necessary t carry out laboratory sensitivity tests with penicillin B i addition to the usual penicillin G.

I. B. R. Duncan

McCarthy, C. G., Hirsch, H. A. & Finland, M. **Serum Levels after Single Oral Doses of 6-(α-Phenoxypropionamido) Penicillinate and Penicillin V.** *Proc. Soc. Exper. Biol. & Med.* 1960, Jan., v. 103, No. 1, 177–80.

A single dose of 250 mgm. of penicillin V, or of alpha-phenoxyethyl penicillin (referred to as penicillin S) was given orally to healthy adults, and penicillin assayed in the blood after 1, 2, 4, 8 and 12 hours by a tube dilution method employing strains of both *Staphylococcus aureus* and *Streptococcus pyogenes*. Only the results after 1, 2 and 4 hours are given, the later specimens having contained no assayable antibiotic. The levels attained, in terms of activity against these 2 organisms, were somewhat higher with V than with S, whether the dose was given before or after a meal. The minimum inhibitory concentrations of these 2 penicillins for the 2 organisms used, in μgm./ml. are stated as streptococcus, V 0·013, S 0·031; staphylococcus, V 0·026, S 0·063. S must therefore have attained higher levels in the blood, but this advantage was rather more than counterbalanced by its lesser anti-bacterial activity.

L. P. Garrod

Holland, S. M., Livesey, E. F., Owen, J., Pennington, G. W., Roberts, J. B. & Somers, G. F. **Blood and Urine Levels following Intramuscular Administration of Potassium Penicillin V.** *Antibiotics & Chemotherapy.* New York. 1960, Jan., v. 10, No. 1, 25–9, 1 fig.

The experiment described in this paper was carried out as a class exercise in the Department of Pharmacology, University of Liverpool. 24 students had an intramuscular injection of 400,000 units of sodium penicillin G, and 24 others had the same dose of potassium penicillin V. Penicillin was assayed in the blood after ¼, ½, 1, 2 and 3 hours and in the total urine passed in 3 hours. In the blood, the level of penicillin G reached a higher initial peak, and fell more rapidly, so that at 3 hours the level of penicillin V was higher. The average percentages of the dose excreted in 3 hours were V 32, G 49. This might merely appear to mean that G was absorbed and excreted more quickly, but the authors suggest, and offer evidence in support, based on a calculation of clearance rates, that the difference is due to the "greater distribution to the tissues" of V. Injections of V caused pain.

L. P. Garrod

Breese, B. B., Disney, F. A. & Talpey, W. B. **Improvement in Local Tolerance and Therapeutic Effectiveness of Benzathine Penicillin. A Comparison of the Effect of Further Purification of the Drug, the Addition of Procaine Penicillin, and the Addition of Prednisolone.** *J. Dis. Children.* Chicago. 1960, Feb., v. 99, No. 2, 149–54. [10 refs.]

"Painful local reactions to benzathine penicillin may be markedly reduced by three methods: (1) further purification of the base used in the manufacture of this drug, (2) the addition of procaine penicillin to the preparation or (3) the addition of 5 mg. of prednisolone. The last method is the most effective in reducing pain and local reaction.

"None of these procedures reduces the therapeutic or prophylactic effect of the benzathine penicillin against β-hemolytic streptococcal infections in children, but, on the contrary, both the purification procedures and the addition of prednisolone seem to improve this effect."

Watson, K. C., Joubert, S. M. & Bennett, M. A. E. **The Occurrence of Haemagglutinating Antibody to Penicillin.** *Immunology.* Oxford. 1960, Jan., v. 3, No. 1, 1–10. [14 refs.]

Siegel, B. B. **Hidden Contacts with Penicillin.** *Bull. World Health Organization.* Geneva. 1959, v. 21, No. 6, 703–13. [20 refs.]

This interesting paper, by an author from New York, discusses 4 ways other than medication by which penicillin may enter the body. It may be present in milk consequent on treatment of cows for mastitis: particulars are given of amounts found in American samples. There is strong circumstantial evidence that sensitized consumers of such milk may react to it (with urticaria etc.), but proof is difficult, although one highly sensitized physician is mentioned who could detect the presence of penicillin in milk by the tingling sensation produced in his mouth by a preliminary sip. Guaranteed penicillin-free milk is now obtainable for such subjects in New York. The author describes tests conducted by himself and M. Walzer to determine the minimum quantity of penicillin taken orally which will elicit a reaction. Direct tests on sensitized subjects were thought inadvisable: instead, their serum, containing "reagins" was injected intradermally into normal subjects, and penicillin in different amounts was given to them, the site of the serum injection being observed for reaction. It was concluded that as little as 40 units, an amount contained in a glass of some of the milk examined, can cause a reaction.

The contamination of syringes with penicillin is another possibility, of which an illustrative case, fully investigated, is cited. A syringe which had been used for administering penicillin needs repeated rinsing, after which the plunger and barrel must be separated before they are boiled, and the water in which they are boiled must be changed "frequently and completely". It would be better to keep a separate sterilizer and syringes for this purpose, or to use disposable cartridges. Penicillin may be inhaled by nurses, pharmacists, and by anyone who happens to be near when it is being administered by aerosol. The fourth and final of the "hidden sources of contact" mentioned, is the now well-known hazard due to the presence of penicillin in poliomyelitis vaccine. The author deals principally with the risks involved here to already sensitized individuals, but points out that such contacts, particularly if long continued, may also sensitize.

L. P. Garrod

BECKER, R. M. **Penicillinase Treatment of Penicillin Reactions.** *Practitioner.* 1960, Apr., v. 184, No. 1102, 447–52, 2 figs. [12 refs.]

"Penicillin is still the most important and effective antibiotic available today. Since the advent of penicillinase, penicillin reactions have been over-emphasized in the lay and medical literature. Because of this physicians and patients are becoming more and more reluctant to use or be given penicillin.

"Penicillinase hydrolyzes penicillin to penicilloic acid which is non-antigenic in a patient having a penicillin reaction. By its removal of the antigen, penicillinase has proved to be a valuable adjunct in treatment of penicillin reactions. Initial clinical studies have shown penicillinase alone to be effective. With the addition of steroids, however, in average doses for three to four days, the patients are more comfortable more quickly.

"Since we cannot be sure which early mild penicillin reaction may not progress to a more serious systemic form, it is recommended that penicillinase be given to every patient with a penicillin reaction. The earlier it is given the more rapid and complete will be the response.

"Case reports are given in which the administration of penicillinase was the turning point in the patient's recovery."

WICK, W. E., HOLMES, D. H. & BONIECE, W. S. **Anti-penicillinase Serum: Use in Treatment of Resistant Staphylococcal Infections in Laboratory Animals.** *Antibiotics & Chemotherapy.* New York. 1960, Feb., v. 10, No. 2, 71–7. [24 refs.]

Rabbits were immunized with a commercial preparation of penicillinase derived from *Bacillus cereus*. The anti-penicillinase content of their serum was measured: its activity against *B. cereus penicillinase* was 8 times greater than that against staphylococcal penicillinase. A dose of this serum was given intraperitoneally to mice: 2 hours later they were inoculated intravenously with a penicillinase-forming staphylococcus, and penicillin treatment (subcutaneous) was begun half an hour before, or 2 or 5 hours after inoculation, and continued daily. The effect was judged by enumerating viable staphylococci in homogenates of kidneys after 2, 3 and 4 days. When penicillin was given before inoculation, these counts were "<10" on each day: when it was first given 2 hours after inoculation the counts were a few thousands: when it was first given 5 hours after inoculation they were in millions, not differing from those in controls given normal instead of immune serum, or no penicillin. [These findings suggest that anti-penicillinase serum is useless after staphylococci have begun to multiply in the body, but they appear to need confirmation with serum containing antibody to staphylococcal penicillinase itself.] Some experiments were also done in rabbits, the results being judged only by survival time. Of 3 groups all treated with penicillin, the average survival time in actively immunized was 25 days, passively immunized 15, and not immunized 4 days. *L. P. Garrod*

HIRSCH, H. A. & FINLAND, M., with the technical assistance of Clare WILCOX. **Comparative Activity of Four Tetracycline Analogues against Pathogenic Bacteria** *in vitro*. *Amer. J. Med. Sci.* 1960, Mar., v. 239, No. 3, 288–94.

"On the basis of simultaneously performed tests of *in vitro* susceptibility of a large number of strains of various human pathogenic bacteria, demethylchlortetracycline appears to be generally more active than any of the other 3 tetracycline analogues now available."

BERTI, T., FASSINA, G. & VECCHIA, P. Influenza di antibiotici sulla desossiribonucleasi dello *Staphylococcus aureus*. [**The Action of Antibiotics on Deoxyribonuclease from** *Staphylococcus aureus*.] *Giorn. di Microbiol.* Naples. 1959, July–Sept., v. 7, No. 3, 173–86, 2 figs. [20 refs.] English summary.

This is a study of the action on deoxyribonuclease of tetracycline, which inhibits protein metabolism in the bacterial cell, of that of chloramphenicol, which in concentrations inhibiting protein synthesis appears also to alter that of nucleic acids [this *Bulletin*, 1958, v. 33, 976] and of that of penicillin which does not seem basically to affect bacterial protein metabolism.

The Oxford staphylococcus was used; deoxyribonucleic acid was extracted from calf thymus by the method described by KAY *et al.* (*J. Amer. Chem. Soc.*, 1952, v. 74, 1724). A litre of broth was seeded with a 24-hour growth and centrifuged at 5000 r.p.m. after 15 hours at 37°C. The deposit was resuspended in 250 ml. of heart-brain infusion broth and distributed in flasks containing varying antibiotic dilutions. Dry weight estimations, viable counts and enzyme estimations were carried out after 3 hours at 37°C. The determination of extracellular deoxyribonuclease was carried out by the method of LASKOWSKI and SEIDEL (see *Arch. Biochem.*, 194[illegible] v. 7, 465); that of the intracellular enzyme was made on extracts of the bacteria obtained by suspending them in glycine (3M at *p*H 7·5) kept at 37°C. for 36 hours. The suspension was then centrifuged at 4°C. (8000 g) and the enzymic activity tested on the supernatant by the method referred to above.

Preliminary investigations showed that the relation between the amount of enzyme present in the medium and the bacterial mass showed a sharp fall during the lag phase and then a rise for the whole period of observation (8 hours). During the lag phase while the staphylococcus has synthesizing activity (the mass increasing by 50%) there was no production of enzyme. Increase in the bacterial mass depends mainly on synthesis of nucleal material. Heart-brain infusion was found to stimulate enzyme production.

Tetracycline, even at concentrations so low that they did not affect reproduction and increase, inhibited the production of ribonuclease; chloramphenicol acted similarly when its concentration was so high that it affected bacterial reproduction and increase. Penicillin fostered enzyme production, the bacterium apparently becoming richer in proteins and in the enzyme under its influence. The power of tetracycline and chloramphenicol may depend on a selective effect which they have on adaptive

enzymes. The fact that the synthesis of deoxyribonuclease is markedly affected by the composition of the medium supports the view that it is an adaptive enzyme.

Tests for studying the action of antibiotics *in vitro* did not show this was modified in any way. *E. Agius*

MORRIS, W. E. **Photosensitivity due to Tetracycline Derivative.** *J. Amer. Med. Ass.* 1960, Mar. 12, v. 172, No. 11, 1155–6.

"In a patient with photosensitivity to a new antibiotic, demethylchlortetracycline (Declomycin) hydrochloride, a considerable rise in the number of circulating eosinophils occurred after exposure to sunlight and a significant elevation in the count of circulating eosinophils after moderate exposure to sunlight after four days of treatment with this drug. Administration of antihistamines and steroids may be useful in the control of this condition."

FALK, M. S. **Light Sensitivity due to Demethylchlortetracycline. Report of Four Cases.** *J. Amer. Med. Ass.* 1960, Mar. 12, v. 172, No. 11, 1156–7.

"Of 27 ambulatory patients 4, whose case histories are given, exhibited skin reactions indicative of photosensitivity while being treated with demethylchlortetracycline (Declomycin) for pustular acne and other pyogenic dermatoses."

GRANATEK, A. P., DUDA, Sofia & BUCKWALTER, F. H. **Pharmaceutical Properties and Stability of Kanamycin.** *Antibiotics & Chemotherapy.* New York. 1960, Mar., v. 10, No. 3, 148–56. [11 refs.]

"This paper has presented some aspects of the stability and pharmaceutical properties of kanamycin and kanamycin formulations. Data on solubility, stability when subjected to sterilization, and stability when incorporated into various pharmaceutical forms have been presented. The results indicate kanamycin to be extremely stable chemically and thermally in powder form and in aqueous solution, permitting, under normal storage conditions, products which should have a shelf life in excess of three years."

DAIKOS, G. K., ATHANASIADOU, Maria & DELIGEORGI, Eleni. Empfindlichkeit 231 grampositiver und gramnegativer pathogener Keime gegenüber dem Kanamycin. [**The Sensitivity of 231 Gram-positive and Gram-negative Pathogenic Organisms to Kanamycin**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 3, 215–18, 1 fig. [16 refs.]

The tests described by these authors from Athens were done by a plate dilution method, the medium containing concentrations of kanamycin falling 2-fold from 40 to 0·075 μgm./ml. *Staphylococcus aureus* (94 strains) was the most sensitive species, the majority of strains being inhibited by 1·25 μgm./ml. (but 4 not even by 20 μgm./ml.). *Escherichia coli* (69 strains) was almost equally sensitive, *Proteus* (34 strains) distinctly less so, and *Pseudomonas pyocyanea* much more resistant, only a few strains being inhibited by low concentrations and 16/26 not by the highest concentration used. The numbers of 2 other species tested are too small to be significant. [An unusual feature of these results is the degree of strain variation, with 8-tube differences or more between the most sensitive and most resistant.] *L. P. Garrod*

SOKOLSKI, W. T. & BURCH, M. R. **Synergism of Endomycin and Neomycin.** *Antibiotics & Chemotherapy.* New York. 1960, Mar., v. 10, No. 3, 157–62, 2 figs.

ARCAMONE, F. M., BERTAZZOLI, C., GHIONE, M. & SCOTTI, T. **Melanosporin and Elaiophylin, New Antibiotics from** *Streptomyces melanosporus (sive melonsporofaciens)* **n.sp.** *Giorn. di Microbiol.* Naples. 1959, July–Sept., v. 7, No. 3, 207–16, 4 figs.

This paper describes in detail a streptomycete which was isolated from a sample of soil from a wheat field near Pescara in the Marches, Italy. Originally the authors named this *Streptomyces melanosporus* but they also refer to it as *melanosporofaciens* to avoid confusion with *Actinomyces melanosporeus* described by KRAINSKY in 1914. The streptomycete was found to produce two antibiotics distinguishable by paper chromatography and bio-autography, elaiophylin appearing as a fast moving component. The chemical characteristics of both are given. Melanosporin is an amorphous nitrogenous substance which antagonizes bacteria including *Mycobacterium* species, and fungi, including *Candida albicans*, *D. neoformans* (? *Cryptococcus*), *Epidermophyton floccosum, Tricophyton mentagrophytes*, and *Penicillium* species, and is fairly active on various plant pathogenic fungi. Elaiophylin is a crystalline white solid. It is active *in vitro* mainly on *Staphylococcus aureus* and on *Mycobacterium* species; its antimycobacterial activity is antagonized by serum and by complex media. In the mouse 50 mgm./kgm. doses (100 mgm./kgm. being the tolerated dose intraperitoneally) did not produce any protection.
E. Agius

MYRVIK, Q. N. & LEAKE, Eva S. **Studies on Antibacterial Factors in Mammalian Tissues and Fluids. IV. Demonstration of Two Nondialyzable Components in the Serum Bactericidin System for** *Bacillus subtilis*. *J. Immunology.* 1960, Mar., v. 84, No. 3, 247–50. [10 refs.]

"The bactericidal system for *B. subtilis* occurring in rabbit and human sera has been characterized further by demonstrating that two nondialyzable components participate in this system. Component I from rabbit has been purified approximately 90-fold. Component I from rabbit will form a full bactericidal system with component II from human serum. Component II activity was demonstrated in guinea pig, sheep and dog sera. Lysozyme has been excluded as a participant in this system."

BAUER, D. J. & SADLER, P. W. **The Structure-Activity Relationships of the Antiviral Chemotherapeutic Activity of Isatin β-Thiosemicarbazone.** *Brit. J. Pharmacol. & Chemotherapy.* 1960, Mar., v. 15, No. 1, 101–10, 2 figs. [35 refs.]

"As part of an investigation devoted to the development of new antiviral agents a compound of established antiviral activity has been subjected to systematic structural modification. The structure-activity data so obtained have been used in the design of new compounds, some of which are described. The compound chosen was isatin β-thiosemicarbazone, which has high activity against neurovaccinia infection in mice, and a 4-point parallel-line assay of *in vivo* chemotherapeutic activity has been developed, which has enabled the activity of the derivatives to be determined against isatin β-thiosemicarbazone as a standard. The overall dimensions of the isatin β-thiosemicarbazone molecule appear to be nearly maximal for the retention of high activity, as all substituents in the aromatic ring decrease the activity irrespective of their nature or position. The projection of the $-CS.NH_2$ group in relation to the ring nitrogen was found to be critical, as the α-thiosemicarbazone was inactive. A number of modifications of the side-chain were investigated: all led to reduction or loss of antiviral activity. The antiviral activity showed a positive correlation with chloroform solubility over a considerable range. The most active compound encountered was 1-ethylisatin β-thiosemicarbazone, with an activity of 286 (isatin β-thiosemicarbazone ≡100). Isatin β-thiosemicarbazone showed no activity against 15 other viruses, and 20 related compounds showed no activity against ectromelia."

MUROMA, A. **The Bactericidal Action of the Rare Earth Metals. Further Studies.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1959, v. 37, No. 3, 336–40.

This is a brief postcript to a previous, much longer paper by this author [this *Bulletin,* 1959, v. 34, 156] on the same subject. It adds observations on the bactericidal action against 2 species only (*Staphylococcus aureus* and *Shigella dysenteriae*) of the salts of 7 further rare metals, erbium, dysprosium, gadolinium, holmium, thulium, lutecium and terbium. The tables of findings seem somewhat incomplete, but the author regards them as in general confirming his previous conclusion that bactericidal activity varies with ionic radius. *L. P. Garrod*

JENEY, E. & ZSOLNAI, T. Versuche zur Entdeckung neuer Tuberkulostatika. XI. Heterozyklische Farbstoffe. **[Experiments for Discovery of New Tuberculostatics. XIth Communication. Heterocyclic Dyes]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 3, 365–72. [37 refs.] XII. Dicarbonsäurehydrazide und mit ihnen verwandte Verbindungen. **[XIIth Communication. Dicarbonic Acidhydracid and Related Compounds]** *Ibid.,* 373–9. [12 refs.]

The English summaries appended to the papers are as follows:—

XI. "The authors investigated the in vitro demo strated tuberculostatic effect of 31 heterocyclicorgan dyes and studied the toxicity exercised upon white mi of 9 compounds, which they found to be the mo efficient. The most important tuberculostatic effect w shown by rivanol, trypaflavin, brilliant-cresyl-blue, nil blue and thionin. The tuberculostatic effect in vitro these compounds was nearly or quite as good as th of dihydrostreptomycin, but did not equal the effe of isonicotine acid-hydracid or 4-aminosalicylacid.

"The most efficacious compounds caused a conside able toxicity in mice, thus appearing a priori unsuitab for therapeutic influence on the tuberculous infectio of the test animals."

XII. "The authors examined in vitro as well as in viv the tuberculous effect of hydracids and phenylhydraci of some dicarbonic acids and ketocarbonic acids. The could state that none of the examined compounds cou exercise either in vitro or in vivo any anti-tuberculo effect. The authors concluded therefrom that the an tuberculous effect of hydracid and phenylhydracid highly structure specific to malein acid and phtal aci as the compounds chemically related to those proved be without any effect."

PFLAUM, W. & v. REICHE, L. K. Vergleichende Untersuchungen an Dampf-Desinfektions-Geräten verschiedener Bauart. **[Comparative Studies of Steam Disinfectors of Different Construction]** *Gesundheits-Ingenieur.* 1959, Dec. 10, v. 80, No. 12, 349–60, 8 figs.

The authors of this paper are engineers in the Technic University of Berlin. They carried out tests of 8 stea disinfectors, 2 of old, and 6 of more modern type, whic are used for clothing, blankets, pillows and mattresse These are divided into 3 classes, according to wheth there is forced circulation in the chamber, and if s whether the direction of the flow is controlled. All ha steam jackets and in all steam was admitted to the cham ber, displacing air, but the temperature intended to b attained is not always specified: some of the charts runs show a rise to 110°C. or even more (this would cau severe shrinkage of blankets and mattresses). No ba teriological tests were done: the method was to inse thermocouples in 12 different positions in the load, whic gave a continuous record of temperature at these point For each machine there is a diagram showing its constru tion and the nature and position of each item in the loa and the position of the thermocouples, together with chart of the temperatures attained. At many points i some machines these rose very slowly, so much so tha in the normal operation time disinfection is unlikely t have been complete.

[The conclusions drawn are about the merits of diffe ent designs, and little is said about loading. In the machin which performed best, mattresses and other items a shown hanging vertically, apparently from a rail, wit spaces between them. In others mattresses, etc., wer piled one on another as many as 8 deep: adequat penetration of such a load is not to be expected. On load contained a bucket standing upright: the tempera ture in this had only reached 53°C. at the end of th 65-minute period of disinfection.] *L. P. Garrod*

ROGERS, M. R., KAPLAN, A. M. & COHEN, G. **Disinfection of Raw Feathers for Bedding Material.** *Pub. Health Rep.* Wash. 1960, Feb., v. 75, No. 2, 107–14, 1 chart. [27 refs.]

"A study of regulations in 42 States and the District of Columbia governing the sterilization of feathers revealed great variety. Little or no technical data are available to substantiate some of the sterilization requirements, especially those pertaining to the sterilization of feathers by heat. Some requirements had little or no public health significance, others contained impractical or unnecessary provisions and still others differed markedly with respect to the same item of sanitation. The present investigation was undertaken to elucidate some of the problems confronting the U.S. Army in preparing specifications to assure that feathers purchased for use in bedding materials would be acceptable by sanitation standards. A practical washing, heat-treating, and chemical disinfecting procedure for processing new feathers is described."

DYTRYCH, O. Chemická kontrola povrchové dezinfekce —II. [**Chemical Control of Surface Disinfection II**] *Československ. Hyg.* Prague. 1959, v. 4, No. 8, 491–7. English summary (6 lines).

The author has previously described [this *Bulletin*, 1960, v. 35, 386] a method of determining the effectiveness of disinfection by chemical determination of the amount of disinfectant removed from a treated surface of given area on a swab, and in the present work full procedural details are given for the application of the same method to the chemical determination of Ajatin (dimethyllaurylbenzylammonium chloride), Famosept (phenylmercuric borate) and lysol. Ajatin is determined by adding a known excess of standard silver nitrate solution and back-titrating with ammonium thiocyanate solution in the presence of ferrous ammonium sulphate as an indicator. Famosept in bulk is determined by digestion with nitric acid and determination of mercury with ammonium thiocyanate; in aqueous extracts of swabs it can be determined colorimetrically with diphenylcarbazone. Swabs from metal surfaces except iron give negative results as the mercury forms an amalgam. Lysol is determined by extraction of the cresol into petroleum ether by acidification, followed by transfer to aqueous alkali and subsequent acidification; the cresol is then titrated with standard bromine solution to give a definite excess, which is then converted to iodine with sodium iodide and titrated with sodium thiocyanate solution.

D. J. Bauer

D'ARCA SIMONETTI, A. Ulteriori ricerche sull'azione detergente del tricloroetilene nei procedimenti del lavaggio a secco degli indumenti. [**Further Investigations on the Detergent Action of Trichloroethylene in the Dry-Cleaning Process**] *Igiene e San. Pubblica.* Rome. 1959, Nov.–Dec., v. 15, No. 6, 485–91. English summary (8 lines).

The author points out that in 2 previous papers he has mentioned that (a) trilene in the dry-cleaning process has no disinfectant, but a detergent action [this *Bulletin*, 1956, v. 31, 438], and (b) that if contaminated and uncontaminated clothing are treated at the same time and if the continuous exchange process for recovery of the trilene used takes place, there is a possibility of organisms being transmitted to the uncontaminated material.

Laboratory experiments were therefore carried out to test this, with pieces of silk, wool, crêpe de chine, poplin and rayon artificially infected with 24-hour cultures of *Bacillus megatherium, Escherichia Coli,* and *Staphylococcus aureus* in an apparatus designed to imitate as faithfully as possible the industrial process. The results showed that both previously sterile and also contaminated strips of all the materials used were infected with *B. megatherium* and *Staph. aureus*, but the results were rather less conclusive for *E. coli.*

The author concludes that in the dry-cleaning process even with the latest type of machine using the continuous exchange process it is not possible to sterilize infected garments though a considerable reduction in the counts occurs even when there are grease spots on them, but the possibility of the transfer of organisms from infected to uncontaminated garments remains. This limits materially the value of dry-cleaning of infected clothing.

W. K. Dunscombe.

MILLER, P. B. **Anaphylactoid Reaction to Oral Penicillin.** *U. S. Armed Forces Med. J.* 1960, Apr., v. 11, No. 4, 451–3.

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

FAGUET, M. Lyses bactériophagiques et croissances secondaires alternées d'un staphylocoque (souche Tw). [**Alternate Bacteriophagic Lysis and Secondary Growth of a *Staphylococcus* (Tw Strain)**] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 143–7, 4 figs.

Growth curves drawn from photometric readings of cultures of *Staphylococcus albus* infected with a phage Tw showed cycles of growth followed by lysis alternating 12 times during 100 hours of observation. The phenomenon was observed whether phage was added before or during the period of exponential growth and it seemed

to be independent of the concentrations of phage or bacteria. The speed of multiplication and subsequent lysis slowed down with time. Cultures of other organisms and their phages (*e.g., Proteus vulgaris* and *Shigella*) did not show the phenomenon. The author offers no discussion or explanation. *Janice Taverne*

LACHOWICZ, T. & DOLEZALOWA, Marta. Typowanie bakteriofagowe gronkowców. [**Bacteriophage Typing of Staphylccoccal Strains**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 4, 679–86.

The English summary appended to the paper is as follows:—

"Bacteriophage types of 262 staphylococcal strains isolated from a hospital material (104 strains from surgical cases, 52 from carriers among hospital staff, 106 current cases from the laboratory for drug resistance examination) were determined.

"164 strains were found to belong to the first phage group, 22 to the third and 76 to the mixed type. The present material exhibited no representatives of the second phage group. In the first group, $\frac{1}{4}$ of the strains was made up by penicillin-sensitive strains and $\frac{3}{4}$ by penicillin-resistant ones, whereas the third group showed 90% of penicillin-resistant strains.

"In the first group the phages 52 and 52+ were the most frequent (122) strains. Also 30 strains isolated from carriers and diseased persons were lyzed by the phage 44A."

LACHOWICZ, T. Ocena serologiczna gronkowców wyosobnionych od chorych i nosicieli. [**Serological Estimation of Staphylococcal Strains isolated from Patients and Carriers**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 4, 687–92. [10 refs.]

The English summary appended to the paper is as follows:—

"249 staphylococcal strains from persons with surgical diseases, carriers among surgical staff and from current diagnostic cases were examined using 3 types sera according to Cowan. 86·76% of strains were determined by slide agglutination method, 58·21% of strains corresponding to the first four Oeding's types. The second and fourth serological types were the most frequent (16·86 and 18·87%). Penicillin-sensitive strains were found to prevail in the second serological type, penicillin-resistant ones in the others."

LACHOWICZ, T. Porównanie typowania bakteriofagowego i serologicznego gronkowców. [**Comparison of Bacteriophage and Serological Typing of Staphylococcal Strains**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 4, 693–7.

The English summary appended to the paper is as follows:—

"Bacteriophage and serological methods of typing *Staphylococci* isolated from disease cases, were analyzed. No correlation could be established between the two methods. The conformity amounted to 16·06% becau 31 strains belonging to the first serological type and the same time to the first group of phages corresponde with 36 strains of the first serological type and with 19 strains of the first group of phages.

"Using phage typing all strains under examinatic could be determined whereas specific type sera failed t determine the serological type of 33 strains, which co stituted 13·25% of all strains examined. The resul were similar to those obtained in studies in the staphyl coccal carrier state."

KASHIBA, S., NIIZU, K., TANAKA, S., NOZU, H. AMANO, T. **Lysozyme, an Index of Pathogen Staphylococci.** *Biken's J.* Osaka. 1959, Aug., 2, No. 2, 50–55, 1 fig.

SELLERS, T. F., Jr. & LEMAISTRE, C. A. **Experimenta Staphylococcal Infection in Mice: Observatior on the Effects of Inoculum Size, Strain Varia tion, Penicillin, and Cortisone.** *J. Lab. & Cli Med.* 1960, Feb., v. 55, No. 2, 199–215, 16 figs.

A technique is described for estimating the number o bacteria in various organs. It is used to study the effe of alteration of infecting dose and penicillin and cortisor treatment on animals infected with staphylococci. Orga from animals which survived were removed afte appropriate intervals, homogenized, and pour plates pr pared of suitable dilutions of the homogenate. The ba terial population for the organ was then calculated.

A coagulase positive strain SA 235 produced infectic of low mortality after intravenous infection of 10^7 orga nisms. Bacterial population curves for kidneys showe multiplication during the first week, a steady populatic during the second week followed by a decline. Th spleen showed a rapid increase during the first week fo lowed by a slow decrease. Organisms persisted for up t 90 days. Lung populations were variable. Inocula c 10^5 organisms or lower produced no detectable multipl cation in the kidneys but splenic populations were simila to those produced by 10^7 organisms. Doses of 10^9 orga nisms produced death of all animals between in 5 and hours so that population curves were not obtained bu lung counts were consistently high 1 hour after infectio Heat-killed organisms failed to kill control mice. 1 organisms of a coagulase negative strain also produce 100% mortality although 10^7 organisms had produced n detectable lesions.

Three freshly isolated coagulase-positive strains fro human lessions were next compared. Population curve for kidney, spleen and lungs were similar but death rat differed considerably for the 3 strains.

Administration of cortisone to animals starting befo infection with SA 235 resulted in population curves o a higher level in kidney and lungs and maintainance c high levels. Penicillin alone reduced populations in kid neys and lungs. The cortisone effect eventually ove came the beneficial effect of penicillin when both wer administered together. Results were essentially the sam when treatment was started after the infection had bee established [the sensitivity of strain SA 235 to penicilli is not given]. *M. Patricia Jevons*

AMSTERDAM, D. & SCHNEIERSON, S. S. **Enhancement of Staphylococcal Virulence for Mice by Intraperitoneal Cortisone Acetate, Cholesterol and Lecithin.** [Correspondence.] *Nature.* 1960, Apr. 2, v. 186, 101–2.

LOURIA, D. B. & ROGERS, D. E. **An Analysis of the Effects of Penicillin on an Experimental Infection produced by Penicillin-Resistant Staphylococci.** *J. Lab. & Clin. Med.* 1960, Feb., v. 55, No. 2, 165–81, 9 figs. [27 refs.]

Mice infected with a penicillin-resistant strain of *Staphylococcus aureus* AZ produced similar infection to mice infected with a penicillin sensitive-strain WO. 80-100% of animals infected with AZ and 40–90% of those infected with WO were dead in 14 days; macroscopic renal abscesses were consistently present in 72 hours.

Penicillin treatment of animals infected with the WO strain resulted in recovery of nearly all animals whether treatment was started early or after 48 hours. Large doses of penicillin started within 4 hours of infection by the resistant AZ strain prolonged life and reduced the mortality but this beneficial effect was reduced if treatment was delayed for 24-48 hours.

Colony counts on homogenized kidney tissue from infected untreated animals suggested that both strains behaved similarly. Counts of kidney tissue from mice infected with AZ were uninfluenced by penicillin treatment started 48 hours after infection but showed great variation when treatment was started 4 hours after infection, when the majority showed a reduction in staphylococcal counts and kidney tissue of 16 of 53 animals showed no staphylococci 7 to 29 days after infection. Control animals infected with the sensitive WO strain showed persisting renal infection. Penicillin treatment, regardless of dose or time of starting treatment, eradicated the kidney infection.

In vitro experiments suggested that large tissue populations of the penicillin-resistant AZ strain might inactivate large amounts of penicillin and that a substance in blood or serum enhanced the drug resistance of the strain. There was no evidence of increased resistance to penicillin of organisms isolated from treated mice 1-7 days after infection. *M. Patricia Jevons*

ELEK, Stephen D. *Staphylococcus pyogenes* **and its relation to Disease.**

This book was reviewed on p. 627.

WOODIN, A. M. **Purification of the Two Components of Leucocidin from** *Staphylococcus aureus.* *Biochem. J.* 1960, Apr., v. 75, No. 1, 158–65, 7 figs. [10 refs.]

PANOS, C., BARKULIS, S. S. & HAYASHI, J. A. **Streptococcal L Forms. II. Chemical Composition.** *J. Bacteriology.* 1959, Dec., v. 78, No. 6, 863–7. [16 refs.]

A comparative chemical analysis is given of the streptococcal L phase variant A.E.D. [this *Bulletin,* 1960, v. 35, 287] and the parent non-typable Group A streptococcus. The authors stress the necessity of employing a protective washing procedure with 0·3M sucrose in order to obtain satisfactory analysis of the L form.

Analysis of this washed material showed that the parent cell wall components, rhamnose, glucosamine and muramic acid were absent in the L form. The other notable difference was an increased content of serine and leucine and an absence of ornithine in the L variant compared to the parent streptococcus. *H. Gooder*

STEWART, F. S., STEELE, T. W. & MARTIN, W. T. **The Mechanisms involved in the Production of Red Cell Panagglutinability by Streptococcal Cultures.** *Immunology.* Oxford. 1959, Oct., v. 2, No. 4, 285–94. [17 refs.]

A cell modifying agent (CMA) is described which renders red cells agglutinable by immune serum prepared against red cells treated with influenza virus allantoic fluid. This agent was found in the supernatant culture fluid of all pneumococci tested, most *viridans* streptococci, a few streptococci of Lancefield's Groups A-Q and 1 strain of *Salmonella typhi-murium.* The agent is thought to be a receptor destroying enzyme.

CMA positive cultures rendered cells agglutinable by normal human serum and cross-absorption tests of pooled serum showed that agglutination was due to antibodies to 4 heat stable agglutinations. One of these antigens (Hickey) is present in many supernatent fluids of streptococcal cultures, all of which were CMA-negative, and all staphylococci examined. It is thought to be the non-species-specific antigen of RANTZ *et al.* [this *Bulletin,* 1956, v. 31, 1278] the other 3 antigens were found only in Hickey-negative strains.

The authors suggest that the identification of these antigens may be of importance in defining a species among the *viridans* streptococci and that the detection of antibodies to these antigens might be of value in the diagnosis of subacute bacterial endocarditis.

M. Patricia Jevons

SLADE, H. D. & SLAMP, W. C. **Studies on** *Streptococcus pyogenes.* **V. Biochemical and Microscopic Aspects of Cell Lysis and Digestion by Enzymes from** *Streptomyces albus.* *J. Bacteriology.* 1960, Jan., v. 79, No. 1, 103–12, 6 figs. [20 refs.]

TEPPER, B. S., HAYASHI, J. A. & BARKULIS, S. S. **Studies of Streptococcal Cell Walls. V. Amino Acid Composition of Cell Walls of Virulent and Avirulent Group A Hemolytic Streptococci.** *J. Bacteriology.* 1960, Jan., v. 79, No. 1, 33–8, 1 fig. [19 refs.]

SCHWAB, J. H. & CROMARTIE, W. J. **Immunological Studies on a C Polysaccharide Complex of Group A Streptococci having a Direct Toxic Effect on Connective Tissue.** *J. Exper. Med.* 1960, Mar. 1, v. 111, No. 3, 295–307. [16 refs.]

" A macromolecular complex of C polysaccharide and peptide derived from Group A streptococcal cells produces a multinodular, remittent, and intermittent lesion of dermal connective tissue following a single intradermal injection. This lesion is greatly modified, both in the gross and microscopically, in rabbits hyperimmunized with a Group A streptococcal vaccine.

" The immune serum, absorbed to yield only antibodies against C polysaccharide as indicated by agar diffusion techniques, will precipitate and neutralize the toxic material. This neutralization and *in vitro* precipitation can be inhibited with formamide-isolated C polysaccharide hapten and with *N*-acetylglucosamine, the primary directive group of this antigen. This clearly demonstrates that antibodies against the group-specific C polysaccharide are responsible for resistance to this toxic material.

"The immunological and other properties of the toxic C polysaccharide complex, the fact that it is a product of Group A streptococci, the gross and microscopic features of the experimental lesion produced with this substance, and the observations of the chronic course of the experimental lesion, indicate that this toxic material should be investigated as a possible factor in the pathogenesis of the non-suppurative sequelae associated with Group A streptococci."

WATSON, D. W. **Host-Parasite Factors in Group A Streptococcal Infections. Pyrogenic and other Effects of Immunologic Distinct Exotoxins related to Scarlet Fever Toxins.** *J. Exper. Med.* 1960, Feb. 1, v. 111, No. 2, 255–84, 10 text figs. & 4 figs. on pl. [47 refs.]

This is a long and detailed paper continuing the work of the author and his associates on the effect in rabbits of extracts of Group A streptococci which had been grown in rabbit skin [this *Bulletin,* 1953, v. 28, 986; 1955. v. 30, 635].

Extracts of Group A streptococcal lesions (SLE) from rabbit skins were shown to enhance the effect of sublethal doses of erythrogenic toxin as they had previously been shown to enhance the effect of Gram-negative bacterial toxins and streptolysin O. Histological studies showed that erythrogenic toxin given in a single injection caused marked tissue damage that was more extensive if animals were pretreated with SLE.

Intravenous injections of type 18 SLE produced a marked pyrogenic effect maximal in 3 hours. Daily injections produced immunity as indicated by a return of the temperature to normal in 6 to 7 days. Cross immunization tests with a type 28 SLE showed this to be a specific immunity rather than a non-specific effect characteristic of endotoxins. The pyrogenic activity of SLE 28 (but not SLE 18) was neutralized by commercial scarlet fever antitoxin prepared against the erythrogenic A toxin of the same specificity as SLE 28. SLE prepared from 2 strains of streptococci of all groups other than group A failed to induce a pyrogenic effect.

Purified erythrogenic toxin and SLE produced simila fever curves and both enhanced lethal and tissue damag ing properties of other toxins but neither prepared th skin for a local Shwartzman reaction.

SLE was unsuitable, because of high serum conten for preparation of purified exotoxins. A preparation wa therefore made from strain NY5 grown in a define medium. Electrophoresis showed there were 2 majo components, hyaluronic acid, and a toxin-containing frac tion A which was separated. Agar diffusion analysi identified fraction A with Stocks erythrogenic toxi to which it behaved similarly in pyrogenic effect enhancement of lethality and the Dick Test.

Streptolysin O or S could not be detected in SLE o fraction A but diphosphopyridine nucleotidase [DPNase was present in fraction A and SLE of some types notabl nephrotogenic type 12. It was absent from SLE of th highly toxic type 18 and Stocks erythrogenic toxin Desoxyribonuclease [DNase] however was present i fraction A but absent from the erythrogenic toxin.

Cross immunization tests with the pyrogenic test, o SLE of various streptococcal types identified 3 distinc toxins, A, B and C; the A toxin is the most common The role of these scarlet fever group of toxins produce *in vivo* in modifying host response to injury and to othe toxic reactions such as hypersensitivity is discussed.

M. Patricia Jevons

FIRSHEIN, W. & BRAUN, W. **Effects of Enzymatic Deoxyribonucleic Acid Digests on Population Changes and Deoxyribonucleic Acid Synthesis of Pneumococci.** *J. Bacteriology.* 1960, Feb., v 79, No. 2, 246–60, 10 figs. [24 refs.]

BJERKEDAL, T. & PALMER, C. E. **Competing Forces of Mortality in Long-Term Animal Experiments. Observation on the Interaction between Experimental Tuberculosis and Extraneous Forces.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 246–53 2 figs. [16 refs.]

Experimental studies of infectious diseases in animals commonly include a group of uninfected and untreated animals to provide a measure of mortality from extraneous causes, *e.g.*, adventitious infections. Usually it is assumed that the extraneous causes affect equally the mortality rate of all the groups of the experiment and that these causes are not affected by the experimental procedures. That the validity of this assumption of independent activity should not be taken for granted is shown by a comparison of the mortality rates of guineapigs in experiments conducted by the authors.

In these experiments, groups of guineapigs were infected with graded doses of tubercle bacilli, the size of the groups being 72 in the infected groups and 107 in the normal untreated group in one of the experiments, and 158 in each of the groups in the other experiment. In the untreated group of the first experiment nearly 60% of the animals died from extraneous causes by the 100th week, and nearly 40% had died by the 50th week in the second experiment, and although by this time most of the infected animals had died, inspection of the death

that had occurred by the 5th-10th weeks showed that less animals had died in the groups injected with the smaller inocula of tubercle bacilli than had died in the untreated groups; for example, the deaths in the control group of the second experiment at the 5th week was 7% compared with 5·1%, 2·5% and 1·9% of the 3 lower-inocula groups of the 5 infected groups.

The authors therefore suggest that in the earlier stages of the tuberculous infection, the presence of tubercle bacilli modifies the course of the diseases constituting the extraneous causes of death; it is therefore misleading in attempting to correct for these extraneous deaths in the treated groups to assume that the experimental infection and these other causes of death act independently.

S. R. M. Bushby

RHEINS, M. S. & BURRELL, R. G. **Further Studies on Auto-Tissue Substances in Tuberculous Rabbits.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 213–17, 2 figs.

In a previous paper [this *Bulletin*, 1959, v. 34, 164] the authors reported that antibodies specific for lung tissue could be detected by complement-fixation methods in rabbits injected intraperitoneally with homologous tuberculous lung tissue or with normal lung tissue and killed tubercle bacilli in Freund's adjuvant, but not in rabbits injected with 0·1 mgm. of virulent tubercle bacilli. In their present paper the authors now report that lung-specific antibodies can be detected in tuberculous rabbits provided the infecting dose is 0·5 mgm. or more. The antibodies are transitory being usually detectable only during the 2nd and 3rd weeks.

Attempts were made to determine the role of these antibodies in pulmonary tuberculosis by injecting rabbits with high titre anti-lung serum, 48 hours before the animals were infected with tubercle bacilli, and then examining the lungs 2 weeks later. The effects were somewhat variable but in general the differences between the lungs of animals receiving this immune serum and those not receiving it were in the extent of the epithelioid reaction, the neutrophil reaction and the number of the discernible tubercle bacilli; there were also areas of haemorrhages in these animals not seen in the others. In some animals, the immune serum was first absorbed with the red cells of the test animals to remove possible *iso*-antibodies, or with tubercle bacilli, and the results supported the authors' contention that the lung antibodies may contribute to the infectious process. *S. R. M. Bushby*

MITCHISON, D. A., WALLACE, J. G., BHATIA, A. L., SELKON, J. B., SUBBAIAH, T. V. & LANCASTER, M. C. **A Comparison of the Virulence in Guineapigs of South Indian and British Tubercle Bacilli.** *Tubercle.* 1960, Feb., v. 41, No. 1, 1–22, 1 fig. [26 refs.]

The results of previous investigations had indicated that either the strains of tubercle bacilli isolated in India were less virulent than those isolated in Europe or that the guineapigs differed in susceptibility to the bacillus. The work described in this paper forms part of a plan to compare the virulence of British and South Indian cultures, to investigate the degree of virulence of the Indian cultures and the clinical findings in the patients from whom they were obtained; this paper is concerned only with the first part of the plan. None of the patients had received chemotherapy for more than 2 weeks and the virulence tests were done in 1 strain of guineapig in India and in 2 in Britain.

The tubercle bacilli were from 83 South Indian and 29 British patients. The strains were identified as tubercle bacilli by their cultural characteristics, absence of growth at 22°C., cord formation, production of aryl sulphatase, catalase and niacin, and their sensitivity to thiosemicarbazone; all the strains were sensitive to isoniazid and streptomycin. The assessment of virulence was based on the extent of the disease, the survival time of the animals and the ability to recover the bacilli by culture from the spleens after intramuscular inoculation of 0·1 or 1 mgm. of the cultures.

The results showed that only 30% of the Indian strains were as virulent as the British strains and the remainder were less virulent, the least virulent (27%) producing little more than a local lesion. Although the results were not statistically significant, the Indian guineapigs appeared slightly more susceptible than the British, but these differences are to form the subject of another paper.

In the discussion the authors emphasize that the infectivity of these less virulent strains is unknown and that their high frequency in India may be a reflection of the lower resistance of the South Indians to tuberculosis. They suggest that the attenuation may be a modification imposed on the bacillus by the need to establish the correct balance between the susceptibility of the host and the virulence of the parasite.

[This is a lengthy and involved paper and it should be read in its entirety by those especially interested.]

S. R. M. Bushby

MAUER, H. Untersuchungen zur Wirkungsweise einer oxydativen Fermentreaktion des *B. cereus* und *Mycobact. tuberculosum.* V. Mitteilung. [**Investigation on the Mode of Action of an Oxydative Enzymatic Reaction of** *B. cereus* **and** *Mycobacterium tuberculosis* **5th Communication**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 1, 60–68, 1 fig.

MAUER, H. Über die Wirkung von dehydrierenden Fermentreaktionen des *B. cereus* und die Beeinflussung durch Tuberkel-Bakterien. VI. Mitteilung. [**The Action of Dehydrating Enzymatic Processes of** *B. cereus* **and their Alteration by Tubercle Bacteria. 6th Communication**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 1, 69–82. [29 refs.]

SEVERE, J. L. **Passive Transfer of Resistance to Tuberculosis through Use of Monocytes.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 326–9. [11 refs.]

"Experiments are reported which demonstrate passive transfer of a limited degree of increased resistance to

tuberculosis through use of monocytes from immunized animals. Use of monocytes from normal animals had no effect on resistance. No increased resistance was seen in animals receiving plasma, spleen homogenate, or spleen filtrate obtained from either normal or immunized animals."

Nègre, L., Bretey, J. & Roy, D. Étude de l'allergie à la tuberculine et de l'infra-allergie aux corps bacillaires dans leurs rapports avec la résistance antituberculeuse chez des cobayes vaccinés par ingestion de grosses doses de BCG. [**Study of Allergy to Tuberculin and Infra-Allergy, and their Relationships with Anti-Tuberculous Resistance in Guineapigs vaccinated by Ingestion of High Doses of BCG**] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 1–6.

In previous papers [*Bull. Acad. Nat. Méd.* 1955, v. 139, 288, this *Bulletin*, 1956, v. 31 (1161); 1959, v. 34, 276] the authors showed that guineapigs that do not react to intact killed BCG after the intradermal injection of BCG, are nevertheless resistant to virulent tubercle bacilli. In their present paper the authors describe the results of 4 experiments in which groups of guineapigs (total 35) were vaccinated orally with 50 mgm. BCG on 5 consecutive days. They were later tested with 1:20 tuberculin and those that failed to react to this antigen were then tested with BCG by scarification. 6-10 months after vaccination the animals were challenged with 0·001 mgm. of a virulent bovine strain of tubercle bacilli and they were killed 6-8 weeks later.

The results showed that whereas only 2% of the animals reacted to tuberculin after 2-3 months, 11% after 5 months and only 2% after the 9th month, the number reacting to the dead BCG was 11% after 3 months, 22% after 5 months and only 2% after 7 months. Comparison of the extent of the tuberculosis after challenge in the vaccinated animals and in a similar number of unvaccinated control guineapigs showed that the vaccination afforded a high state of protection irrespective of the degree of the reaction to tuberculin. The extent of this protection was considered to be equal to that afforded by intradermal vaccination, and in the authors' opinion the results of these experiments clearly demonstrate the complete dissociation existing between allergy and immunity.

S. R. M. Bushby

Weissfeiler, J. & Karassova, Valentina. **Study of a Vaccine Strain of** *Mycobacterium tuberculosis*. *Acta Microbiologica.* Budapest. 1960, v. 7, No. 1, 77–86, 6 figs. [13 refs.]

"(i) Strain No 115 is a variant of human *Mycobacterium tuberculosis* with attenuated virulence.

"(ii) The attenuated virulence of strain No 115 did not undergo any change during 4 years' passage in guineapigs.

"(iii) Inoculated into guineapigs, the strain continued to multiply for 4 to 5 months, and could be obtained in cultures from the organs even as late as 236 days following inoculation.

"(iv) Subcutaneous or oral vaccination of guineapi with strain No 115 was followed by an immunity higher order than that brought about by BCG.

"(v) Pathogenicity of strain No 115 in monkeys w found to be attenuated. On the basis of the above, stra No 115 may be considered a vaccinating strain."

Venulet, J., Jakimowska, Krystyna, Janowiec, M. Urbanska, Alicja. **The Accumulation of Isoniaz in Tissues, and the Course of Experiment Tuberculosis.** *Brit. J. Pharmacol. & Chem therapy.* 1960, Mar., v. 15, No. 1, 4–9, 6 figs. [refs.]

Davies, G. E. & Driver, G. W. **Action of Two Eth Thiol Esters against Experimental Tuberculos in the Guinea-Pig.** *Brit. J. Pharmacol. & Chem therapy.* 1960, Mar., v. 15, No. 1, 122–7.

"Two thiol esters, ethyl dithiolterephthalate (Cor pound 13,130) and ditophal (ethyl dithiolisophthalat Etisul), have been tested for their antituberculosis activi in guineapigs. Compound 13,130 was active at a dose 100 mg./kg. twice daily by mouth in animals infecte subcutaneously, but was inactive against an intracerebr infection at 50 mg./kg. Ditophal was active in the su cutaneously infected animals at 200 mg./kg. orally or mg./kg. subcutaneously. Higher doses subcutaneous were irritant."

Tacquet, A., Macquet, V., Buu-Hoi, N. & Da Xuong, N. Étude *in vitro* et *in vivo* de l'activi antituberculeuse de la 4-4′ diisoamyloxythiocarban lide. [**Studies** *in vitro* **and** *in vivo* **of the Ant tuberculous Activity of 4-4′ diisoamyloxythi carbanilide**] *Ann. Inst. Pasteur de Lille.* 1958 1959, v. 10, 43–50. [10 refs.]

Tacquet, A., Andrejew, A. & Macquet, V. Pouvo pathogène pour la poule et le lapin des myc bactéries aviaires résistantes à de fortes concentra tions d'isoniazide. [**Pathogenicity for Fowls an Rabbits of Avian Mycobacteria Resistant to Hig Concentrations of Isoniazid**] *Ann. Inst. Pasteur Lille.* 1958–1959, v. 10, 29–36, 1 pl.

Andrejew, A. Étude des activités catalasique et peroxy desique des mycobactéries aviaires, en fonction leur résistance à l'I.N.H. [**Catalase and Perox dase Activity of Avian Mycobacteria in Relatio to Isoniazid Resistance**] *Ann. Inst. Pasteur Lille.* 1958–1959, v. 10, 37–41, 1 fig.

Marks, J. & Trollope, D. R. **A Study of th "Anonymous" Mycobacteria. I. Introduction Colonial Characteristics and Morphology; Growt Rates; Biochemical Tests.** *Tubercle.* 1960, Feb v. 41, No. 1, 51–62. [21 refs.]

The 114 strains were from cultures of sputum exar ined from 1952 to 1959, during which time 200,000 spec mens were cultured and 16% were positive for tuberc

bacilli; the incidence of anonymous strains in the 6,000 positive cultures from new cases was 2%. Almost all the strains were recognized initially to be distinct from tubercle bacilli by their morphology, being either shorter or longer than tubercle bacilli, their soft or coloured colonial form, their growth at 25°C. or their high resistance to the antituberculous drugs. 51 of the strains were regarded as pathogenic because they had been isolated on more than 1 occasion and the others were regarded as casual.

Almost half the pathogenic strains were non-chromogens, *i.e.* the growth was cream or buff irrespective of whether they were exposed to light. Only a few of the photochromogens were casual strains but most of the scotochromogens were casual. The strains that grew as exceptionally long bacilli were mostly photochromogens while most of those that grew as the short bacilli were either scotochromogens or non-chromogens. The colonial form of about 33% of the strains was similar to that of the tubercle bacillus, and the non-chromogens that grew in this form could not be identified without further tests.

In Dubos-plasma none of the strains showed cording, but some showed slight cording on egg medium. Although the use of Lemco-peptone broth, egg medium and thioglycollic medium confirmed that these bacilli are less fastidious than the tubercle bacillus, they were less valuable for identifying freshly isolated cultures as many of the strains grew poorly on these media. All but 2 of the strains, both scotochromogens, failed to grow in 4 weeks on egg medium at 25°C., but some grew at 44°C.

The arylphosphatase was of value for differentiating the bacilli from the tubercle bacillus if small inocula were used and if the concentration of the substrate was 5 mM, a concentration which discourages the growth of the tubercle bacillus. Provided the growth was plentiful, a negative or a positive-trace niacin test was of value in identifying these strains. Most of the strains were catalase positive. [The authors recommend that this test be done on media containing 5 μgm. isoniazid per ml., as a positive test will then exclude the tubercle bacillus.] A strongly positive peroxidase test was given only by tubercle bacilli, and only 1 anonymous strain was strongly neutral red positive. Tests for urease activity and redox dye reduction did not prove of much value.

S. R. M. Bushby

CSILLAG, Anna. **Periodic Acid-Schiff (PAS) Staining of "Atypical" Mycobacteria and Tubercle Bacilli.** *Tubercle.* 1960, Feb., v. 41, No. 1, 63–7, 1 fig. [14 refs.]

The cultures examined were 24 strains of tubercle bacilli, 37 strains of "atypical" acid-fast bacilli and 4 other named species, which included 2 saprophytes, and as they all showed some degree of pink or red staining the films were stained with malachite green, a procedure which removed some of the redness from the more weakly positive ones.

The quantity of material in the bacilli staining with the periodic-acid-Schiff technique varied with the age of the culture and the medium; it was most plentiful in the bacilli after 14-17 days' incubation in Kirchner medium and there was less in the bacilli grown on Löwenstein-Jensen medium. The most strongly positive strains were the photochromogens and the scotochromogens, but in the author's opinion they had examined too few strains for a true assessment to be made of the value of this stain for differentiating mycobacteria.

S. R. M. Bushby

TYSAROWSKI, W. & KWIEK, S. **Difference between the Catalases of Acid-Fast Bacilli.** [Correspondence.] *Nature.* 1959, Nov. 7, v. 184, Suppl. No. 19, 1513–14, 1 fig.

The tubercle bacillus becomes catalase-negative when it becomes highly resistant to isoniazid but the saprophytes retain at least some catalase-activity when they become resistant. In this letter the authors report that measurements of the catalase-activity of washed suspensions of H37Rv and of *Mycobacterium smegmatis* in the presence of sodium azide indicate that there are at least 2 different catalase enzymes in acid-fast bacilli. The measurements show that whereas the catalase present in the virulent acid-fast bacilli has activation energy of 9400 cal. (500 σ), the activation energy of that of the saprophyte is only 4300 cal. (500 σ), and in the presence of 10^{-6} M. solution of sodium azide the catalase-activity of the tubercle bacillus was only reduced by 5% whilst that of the saprophyte was reduced by 84%. The catalase of the saprophyte is therefore "azide-sensitive" but isoniazid-resistant.

The authors suggest that the saprophytes possess both enzymes, but not in equal proportions, so that when they become resistant to isoniazid and lose only the drug-susceptible catalase they are still catalase-positive, but when the tubercle bacillus which has only the drug-susceptible catalase develops resistance to isoniazid it becomes catalase-negative. *S. R. M. Bushby*

KUBICA, G. P. & POOL, G. L. **Studies on the Catalase Activity of Acid-Fast Bacilli. I. An Attempt to Subgroup these Organisms on the Basis of their Catalase Activities at Different Temperatures and pH.** *Amer. Rev. Respiratory Dis.* 1960, Mar., v. 81, No. 3, 387–91. [20 refs.]

"The catalase activity of 100 stock and recently isolated wild strains of acid-fast bacilli has been determined at room temperature and at 68°C. With the exception of 4 isoniazid-resistant human strains, all cultures of acid-fast bacilli exhibited positive catalase activity at room temperature.

"It was found that the catalase enzyme of human and bovine strains (regardless of virulence) was inactivated by suspending the cultures in a phosphate buffer of pH 7 which was then held in a 68°C. water bath for 20 minutes. All other cultures tested retained their catalase activity under these conditions.

"It is suggested that, pending further studies on wild strains, this modified catalase test may prove useful as a means of subgrouping the acid-fast bacilli."

BÖNICKE, R. Über das Vorkommen von Acylamidasen in Mycobakterien. III. Mitteilung. Der enzymatische Abbau von Allantoin. [**The Occurrence of Acylamidases in Mycobacteria. IIIrd Communication: Enzymic splitting of Allantoin**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 2, 186–94, 5 figs. [10 refs.]

TARABINI CASTELLANI, J. Bacteriología de la infección hanseniana. [**Bacteriology of Leprosy**] *Rev. "Fontilles"*. Alicante. 1959, July–Dec., v. 4, No. 8, 685–702.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 711.]

ITO, T. & SONODA, R. **Biochemical Studies on the Murine Leprosy Bacillus. II. Respiration and Respiration Accelerating Substances.** *Biken's J.* Osaka. 1958, Dec., v. 1, No. 2, 157–65. **III. Enzymatic Activity.** *Ibid.*, 166–72, 2 figs. [10 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 715.]

MALFATTI, M. Aplicación de la técnica del sombreado al estudio del *Mycobacterium leprae*. [**Application of the Shading Technique to the Study of** *Mycobacterium Leprae*] *Semana Méd.* 1959, Dec. 10, v. 115, No. 24, 948–57, 12 figs. [25 refs.] English summary.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 711.]

BAGDASARIAN, G., HULANICKA, Danuta, KLECZKOWSKA, Hanna, KŁOPOTOWSKI, T. & WIATEROWA, Alina. Badania nad metabolizmem maczugowców błonicy. Doniesienie I. Oddychanie w obecności różnych substratów. [**Studies on the Metabolism of** *C. diphtheriae*. **I. Respiration on Different Substrates**] *Med. Dośw. i Mikrob.* Warsaw. 1959, v. 11, No. 2, 85–91. [15 refs.] Doniesienie II. Wpływ cyjanku na oddychanie maczugowców błonicy. [**II. The Effect of Cyanide on the Respiration of** *C. diphtheriae*] *Ibid.*, 93–102, 2 figs. English summary.

The effect of various carbohydrates and other substances on the oxygen uptake of the PW8 strain of *Corynebacterium diphtheriae* has been investigated. Monosaccharides were utilized more readily than disaccharides, and also 2 of 5 fatty acids (acetic and propionic) and certain components of the citric acid cycle. The respiration of the organisms in the presence of carbohydrates and other substrates of the glycolytic cycle was strongly inhibited by cyanide in a concentration of 10^{-4}M.

D. J. Bauer

RELYVELD, Edgar H. Toxine et antitoxine diphtériqu Étude immunologique. [**Immunological Study Diphtheria Toxin and Antitoxin**] 164 pp., 58 fi 1959. Paris VI: Hermann, 115, Boulevard Sai Germain. [24 NF.]

This is an extensive and masterly review of the wo on diphtheria toxin-antitoxin in which the author been concerned for several years.

Actually, a great deal of the work on which the pa is based has already been published in one form another and, notably, in the colloquium of the Fre Society of Microbiology, in June, 1959. The book w therefore, be reviewed rather briefly.

In the first chapter there is a detailed description the medium which has ultimately been found to be b for toxin production. This medium is composed of cas hydrolysates but, in other respects, it is a defin medium. Special attention is drawn to the method ensuring an iron content of 160 μgm./litre, the optim varying slightly with different samples of casein dige Cultures grown for 8 days in this medium should give titre of 1,320 flocculating units per mgm. of prot nitrogen.

In the second chapter the concentration of the toxin bulk by phosphate and ammonium sulphate precipitati or in smaller amounts by chromotographic methods, described; also the method of obtaining the separation crystals of toxin from material which has undergone initial concentration by either of these methods.

In a further chapter, the various methods available antigenic analysis by diffusion into agar are descrit and the underlying principle of each is discussed. Th are the methods of (a) Oudin-diffusion of antigen in fl solution to a gel in which there is uniform distributi of antibody; (b) diffusion of antigen and antibody to interposed column of gel (method of OAKLEY and F THORPE, [this *Bulletin,* 1953, v. 28, 656]) its modificati to make it applicable to several antigens diffusing towa a single antibody or *vice versa,* as adopted by Ouchte lony; and finally, the methods of immunoelectrophore This is perhaps the most useful chapter in the book.

In a study of the quantitative aspects of the toxin-a toxin reaction, it is shown that curves indicating amount of precipitate appearing as the concentration antigen is increased may take one or two forms. In first, precipitation occurs from the outset, rises to rat sharp maximum and then falls rapidly. This is descril as the rabbit or precipitin type of curve. In the seco the precipitate does not appear at first since it is solu in excess of antibody. It rises sharply and then contin to rise more gradually as a straight line, to fall a rapidly in excess of antigen, in which the precipitat also soluble. This type of curve is described as the fl culation or horse type.

The comparison of such observations with those immunoelectrophoresis shows, however, that the dif ence in the appearance of the curves does not depend the animal used so much as on the type of globu which is carrying the antibody. In other words, the r bit type of curve is obtained with sera in which the a body is mainly located in the gamma globulin wher the curve of the horse type depends on the use of s

n which the antibody is mainly located in the β_2 lobulin.

The great majority of sera produced in the antitoxin aboratories are from hyperimmunized horses which had basic immunity at the outset of hyperimmunization. n such sera the antibody is mainly located in the β_2 lobulin fraction. Finally, the grounds for supposing he toxin to be a large molecule with multiple antigenic acets, of which one only is toxic and stimulates the pro- uction of neutralizing antibody are set forth, as has lready been done in the Colloque Annuel de la Société rancaise de Microbiologie. (1re Journée: 11 Juin 1959. *roblèmes généraux d'immunologie*). *J. W. McLeod*

GUNDERSEN, W. B. & HENRIKSEN, S. D. **Conversion in *Corynebacterium belfanti* by means of a Temperate Bacteriophage originating from a Toxigenic Strain of *Corynebacterium diphtheriae*, Type *mitis*.** *Acta Path. et Microb. Scandinavica.* 1959, v. 47, No. 2, 173–81. [15 refs.]

The ability of *Corynebacterium diphtheriae* strains to roduce toxin is known to result from phage conversion. t was confirmed that resistant colonies derived from ion-toxigenic strains incubated with the temperate phage β_2 were lysogenic and toxigenic.

C. belfanti, which differs from *C. diphtheriae* in being nable to produce toxin or to reduce nitrates to nitrites, vas not apparently lysogenic. Phage β_2 did not form laques on it, though there was evidence that the phage vas absorbed. When 7 strains of *C. belfanti* were treated vith β_2 and cultured on Elek plates, it was found that high proportion of colonies had become toxigenic. All hese colonies were now also lysogenic and had acquired he ability to reduce nitrates. Thus they could not be listinguished from *C. diphtheriae*. The authors remark hat the abilities to produce toxin and to reduce nitrates eem to be linked, and discuss possible mechanisms of inkage. *Janice Taverne*

ERRATUM

In the abstract of the paper by POPE and STEVENS, his *Bulletin*, 1960, v. 35, 393, the formula for sodium ulphite should read Na_2SO_3, not $Na_2S_2O_3$ as printed.

WHEAT, R. W. & PITTMAN, Margaret. **Degradation of Certain Nucleotides by *Haemophilus influenzae* and *Haemophilus aegyptius*.** *J. Bacteriology.* 1960, Jan., v. 79, No. 1, 137–41. [18 refs.]

EAGON, R. G. & WILLIAMS, A. K. **Enzymatic Patterns of Adaptation to Fructose, Glucose, and Mannose Exhibited by *Pseudomonas aeruginosa*.** *J. Bacteriology.* 1960, Jan., v. 79, No. 1, 90–94, 1 fig.

JOÓ, I. & PUSZTAI, S. Die Massenzüchtung pathogener Darmbakterien. II. Mitteilung: Immunbiologische Untersuchungen. [**Mass Cultivation of Pathogenic Intestinal Bacteria. 2nd Communication: Immunobiologic Investigations**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 1, 51–9. [23 refs.]

UETAKE, H. & HAGIWARA, S. **Somatic Antigen 15 as a Precursor of Antigen 34 in *Salmonella*.** [Correspondence.] *Nature.* 1960, Apr. 16, v. 186, 261–2.

CAREY, W. F. & BARON, L. S. **Comparative Immunologic Studies of Cell Structures isolated from *Salmonella typhosa*.** *J. Immunology.* 1959, Nov., v. 83, No. 5, 517–20. [14 refs.]

With the 2 typhoid strains, Ty 2, and 0·901 isolated cell walls, protoplasts and protoplasmic membranes were prepared in order to determine the comparative toxicity, antigenic structure and vaccine potency of the isolated cell structures.

The toxicity of the cell walls of the 2 strains, expressed as LD50 values, was approximately the same; that of the intact bacterial cells also gave the same figure when tested in mice. Isolated protoplasts and protoplasmic membranes were less toxic. Both somatic antigen fractions, 9 and 12, were represented in the protoplasts and membranes. The mouse protective efficiency of protoplasts of strain Ty 2 depended on the presence of Vi antigen in the protoplast vaccine. It is also of interest to note that the non-Vi strain 0·901 protoplasts could absorb purified Vi antigen isolated from *Escherichia coli* 5396/38 and retain it whereas intact cells or protoplasmic membranes similarly treated failed to adsorb the antigen. The Vi treated 0·901 protoplasts showed specific Vi agglutination of much the same order as the Ty 2 protoplasts.

H. J. Bensted

ENGLESBERG, E. **Inhibition of the Growth of *Salmonella typhosa* by L-Rhamnose.** *J. Bacteriology.* 1960, Jan., v. 79, No. 1, 58–64, 5 figs.

MATĚJOVSKÁ, D., JELÍNEK, J. & RASKA, K. K otázce experimentálního hodnocení očkovacích látek proti tyfu a paratyfům. [**The Question of Experimental Evaluation of Vaccines against Typhoid and Paratyphoid Fever. Part III**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 5, 299–303, 2 graphs. [16 refs.] English summary (8 lines).

In comparative protection tests of an alcohol-treated and a formolized typhoid vaccine mice were given doses of the vaccine ranging from 10 million to 1,000 million organisms and were then challenged with a virulent strain of *Salmonella typhi* in serial 1·8-fold dilutions ranging from 18 to 550 LD50. The challenge dose in LD50 resisted by the mice had a linear regression against log dose of vaccine, but the regression coefficient of the alcohol vaccine was lower than that of the formolized vaccine and the 2 lines intersected, so that the relative efficacies of the 2 vaccines depended upon the dose used for vaccination. *D. J. Bauer*

RIBI, E., HOYER, B. H., MILNER, K. C., PERRINE, T. D., LARSON, C. L. & GOODE, G. **Physical and Chemical Analysis of Endotoxin from *Salmonella enteritidis*.** *J. Immunology.* 1960, Jan., v. 84, No. 1, 32–47, 2 figs. [33 refs.]

The endotoxin released from cells of *Salmonella enteritidis* with aqueous ether and refined by dialysis or by

precipitation with 68% ethanol is composed of protein (14-30%). lipid (2-12%) and polysaccharide. The sugars in the polysaccharide are glucose, galactose, mannose and rhamnose in equal concentration. It is also confirmed that major portions of the protein moiety of an endotoxin can be removed without destroying its toxic or antigenic properties. *H. J. Bensted*

Biozzi, G., Howard, J. G., Halpern, B. N., Stiffel, C. & Mouton, D. **The Kinetics of Blood Clearance of Isotopically Labelled *Salmonella enteritidis* by the Reticulo-Endothelial System in Mice.** *Immunology.* Oxford. 1960, Jan., v. 3, No. 1, 74–89, 9 figs. [22 refs.]

Rudner, Rivka & Balbinder, E. **Reversions induced by Base Analogues in *Salmonella typhi-murium*.** [Correspondence.] *Nature.* 1960, Apr. 9, v. 186, 180.

Raettig, H. Provokation einer Infektion durch Schutzimpfung. 4. Mitteilung. Provokation während der experimentellen *S. typhimurium* Epidemie nach vorangegangener Immunisierung. [**Provocation of Infection by Vaccination. 4th Communication: Provocation during the experimentally caused *S. typhi-murium* Epidemics after Preceding Immunization**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 618–31, 5 figs.

Earlier communications on this subject have been reviewed [this *Bulletin,* 1959, v. 34, 1282 *ter.*] The experimental work now recorded refers to the effect of the administration of a protective vaccine to animals which have consumed fodder infected with *S. typhi-murium* some days before but which had all had a previous immunization against that infection.

The results are too equivocal to permit of a very definite conclusion. *J. W. McLeod*

Chambon, L., Le Minor, L. & Martin, P. Recherche d'entérobactéries chez des animaux à sang froid du Centre- et du Sud-Vietnam. [**Enterobacteria in Cold-Blooded Animals in Central and South Vietnam**] *Bull. Soc. Path. Exot.* 1959, Nov.–Dec., v. 52, No. 6, 720–23.

The following is a translation of the authors' summary:—

32 strains of *Salmonella,* of 8 serological types (2 hitherto unknown in Vietnam—Salm. Tananarive and Salm. Uganda) were isolated from snakes and lizards [in South Vietnam]. 69 strains of Arizona were also isolated, some belonging to 5 new serotypes:—21: 1, 2, 5, 6; 9:29-31; 16:33, 25; 16:39, 25; and 29:33-40.

Charles Wilcocks

Novgorodskaia, E. M. **Considerations on the Classification of the Dysentery Bacilli.** *J. Microbiol. Epidemiol. & Immunobiol.* London. 1959, v. No. 4, 7–17, 3 figs. [Translated from Russian.]

The U.S.S.R. system for the classification of the dysentery bacilli follows the general principles of the International scheme, but the serotypes included in sub-groups A, B and C are somewhat different. Sub-group A comprises only the Grigor'eva Shiga and the Stutzer Schmorganisms; the Large-Sachs bacilli are not included. The Flexner sub-group has different symbols: *Sigella flexn* 1 a (V) is known as Flexner f. The Boyd sub-group the name "Boyd-Novgorodskaia" and contains serotyp not in the International list and does not include all our types. Moreover the symbols for the types in sub-group are Roman numerals which do not correspo with our Boyd 1, 2, 3 etc.

The author is familiar with the international literature dealing with the classification of the dysentery bac and is herself an experienced intestinal bacteriolog Although the incidence of serious bacillary dysentery the U.S.S.R. has been much reduced in recent years it still an important problem to the health authorities remote areas and it was always expected that additio antigenic types belonging to Boyd's sub-group C wo eventually be revealed in more extensive surveys. It now well over 20 years since Sir John Boyd describ his new types of mannite-fermenting dysentery bac that were to be found in his collection of cultures fr Indian sources. It is remarkable that since that time various surveys in different parts of the world ha revealed so few additional types even if the few new o now reported from the U.S.S.R. are included. It is to hoped that an increase in the availability of informati of this nature from the U.S.S.R. will enable a number small differences of nomenclature and classification to ironed out eventually. *H. J. Bensted*

Michael, J. G. & Braun, W. **Modification of Bactericidal Effects of Human Sera.** *Proc. Soc. Exp Biol. & Med.* 1959, Nov., v. 102, No. 2, 486–90.

Growth of bacteria in broth media of different co position was found to alter their subsequent suscep bility to antibody- and complement-containing hum serum. Altered sensitivity was also obtained when bactericidal system was directly supplemented with diff ent concentrations of various growth media.

It was found that low concentrations of broth, gluc and certain amino acids, known to promote metaboli increased bacterial susceptibility to human serum wh certain strains of *Shigella dysenteriae* and *Escheric coli* were examined. On the other hand, metabolic inh itors—5-methyltryptophan, fluorophenylalanine and n bactericidal concentrations of chloramphenico decreased bacterial susceptibility to human serum. Wh bacteria were incubated with so-called basic amino ac in buffer, the protective-effect was removed by sim washing in saline before serum treatment, but if nutrie such as tryptose broth, were present during exposure the relatively high concentrations of basic amino ac the protective effect was not removed by washing.

H. J. Benstec

Cooper, G. N. & Pillow, Jill A. **An Immunologic Comparison of Cell Components of** *Shigella dysenteriae* **Type 2.** *J. Immunology.* 1960, Feb., v. 84, No. 2, 135–42. [20 refs.]

Shigella dysenteriae Type 2 was selected for these experiments because it is antigenically homogeneous and does not cross serologically with other shigellae. Various isolated cell components were prepared; cell walls, protoplasts, protoplast membranes and cytoplasm and their antigenic make-up was compared with whole bacterial cells. Cell walls and protoplast membranes were found to be serologically homogeneous and indistinguishable from the isolated somatic antigen or endotoxin. Whole bacterial cells, protoplasts and cytoplasm contained at least 2 antigen components, one of which was identical with the somatic antigen, and the other, apparently cytoplasmic in nature, has not been further characterized. Mild alkaline hydrolysis of whole cells or various cell components, followed by acetone precipitation, led to the recovery of material related to the somatic antigen of the original culture.

It was concluded that the somatic antigen is not only localized in the cell wall or on the surface but is distributed throughout the bacterial cell. *H. J. Bensted*

Dashkevich, I. O. & Diakov, S. I. **Type-Specific Staining of** *Shigella flexneri* **using Fluorescent Antibodies.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 4, 53–8. [Translated from Russian.]

The identification of the Flexner organisms by the fluorescent antibody technique has been demonstrated by a number of workers in recent months (this *Bulletin,* 1960, v. 35, 190). This paper deals with experimental trials with cultures of Flexner c (*Shigella fiexneri* 2a (W) in our classification scheme) and the results are in accordance with the experience of others. No new information is noted in the present communication.

H. J. Bensted

Formal, S. B., Dammin, G. J., Schneider, H. & LaBrec, E. H. **Experimental** *Shigella* **Infections. II. Characteristics of a Fatal Enteric Infection in Guinea Pigs following the Subcutaneous Inoculation of Carbon Tetrachloride.** *J. Bacteriology.* 1959, Dec., v. 78, No. 6, 800–804, 1 fig.

Previously a fatal Flexner 2a infection of guineapigs had been induced by oral administration of the infecting organism to starved animals who were given calcium carbonate immediately before the challenge and opium immediately after [this *Bulletin,* 1959, v. 34, 158]. Postmortem examination of the animals showed fatty changes in the livers and it was therefore decided to determine the effect of liver injury caused by other means. This paper reports the effect of injections of carbon tetrachloride. A single dose of 0·15 ml. of the reagent was injected 24-48 hours before the challenge dose of *Shigella flexneri* 2a was administered orally. The calcium carbonate and the opium were given as in the previous experiments. The LD50 for Flexner 2a in these experiments was 10^6 to 10^7 bacterial cells, but other animals receiving *Escherichia coli* or *Salmonella typhi* survived doses in excess of 10^8 cells. Animals dying 24-48 hours after the Flexner challenge showed congestion and ulceration of the large gut and, as the interval between challenge and death increased, the lesions in the large intestine tended to be more extensive. Dysentery bacilli were isolated only from the intestinal tract. *H. J. Bensted*

Kotełko, Krystyna, Szydłowski, S. & Zabłocki, B. Badania nad zmiennością fazową *Shigella sonnei.* Doniesienie I. [**Studies on the Phase Variation of** *Shigella sonnei*] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 1, 53–9.

The English summary appended to the paper is as follows:—

"The following variation forms of Shigella sonnei have been shown: (1) very minute colonies (diameter 0·5 mm) of phase I, (2) colonies of average size (diameter 1·5-2·0 mm) of phase I, (3) intermediate colonies between phase I and phase II, (4) colonies of phase II.

"The first two variants give a positive keratoconjunctivitis reaction in guineapigs.

"Egg medium does not inhibit the process of transition from phase I into phase II. Numerous passages through the conjunctiva of the guineapig's eye limits this process.

"The immunity produced after keratoconjunctivitis proved to be specific, local and temporary."

Mian, K. A. **Isolation of Enteropathogenic** *Escherichia coli* **from Household Pets. Relation to Infantile Diarrhea.** *J. Amer. Med. Ass.* 1959, Dec. 5, v. 171, No. 14, 1957–61, 1 fig.

From rectal swabs collected from 237 domestic dogs and 84 cats, all apparently healthy, 34 and 7 strains, respectively, of enteropathogenic *Escherichia coli* were isolated; they comprised 6,O 111; 13,O 55; 18,O 26; 2,O 127 and 2,O 125 serotypes. The author suggests that outbreaks in children's nurseries are introduced by infected nurses or visiting parents who contracted the infection from a domestic pet.

While this is, of course, quite possible, it is equally possible for the pet to contract the infection from the environment contaminated by the child who might be excreting the particular serotype concerned before the clinical illness became manifest. *H. J. Bensted*

Lemcke, Ruth M. & White, Helen R. **The Heat Resistance of** *Escherichia coli* **Cells from Cultures of Different Ages.** *J. Applied Bact.* 1959, Aug., v. 22, No. 2, 193–201, 3 figs. [13 refs.]

"From the mortality curves of *Escherichia coli* cells heated at 55° in Ringer's solution both Decimal Reduction Times (DRTs) and 99·9% mortality times were obtained. In terms of these measures of heat resistance, cells harvested from broth cultures 0-8 hr old were more

susceptible than those from mature cultures. The time of commencement and the approximate duration of the logarithmic phase of growth of the organism in broth were determined from growth curves, and it was observed that the heat resistance was minimal during that phase.

"Death rates were not always uniform for the whole of a given population. Particularly among young cultures, a period of rapid death was frequently followed by the slower death of a relatively small number of survivors. In one instance only was an initial period of slow death followed by one of more rapid death."

LEMCKE, Ruth M. **The Changes with Age in the Resistance of** *Escherichia coli* **to drying under Atmospheric Conditions.** *J. Applied Bact.* 1959, Aug., v. 22, No. 2, 253–7.

"The resistance to drying under atmospheric conditions of *Escherichia coli* cells suspended in water, broth and horse serum was investigated. Cells from cultures in the early (logarithmic) growth phase were more susceptible than older cells, and this, together with the fact that the strain of *E. coli* used was very sensitive to drying, even in a protective menstruum such as horse serum, made it unlikely that the clearer chromatin staining obtained with cells from young than from old cultures could be attributed to the occurrence of less disruption of the former during drying of the films."

GREISMAN, S. E. **Activation of Histamine-Releasing Factor in Normal Rat Plasma by** *E. coli* **Endotoxin.** *Proc. Soc. Exper. Biol. & Med.* 1960, Mar., v. 103, No. 3, 628–32, 1 fig. [12 refs.]

SZULMAJSTER, J. & WOODS, D. D. **The Synthesis of Methionine from Homocysteine by Enzymic Extracts of** *Escherichia coli*. *Biochem. J.* 1960, Apr., v. 75, No. 1, 3–12, 4 figs. [29 refs.]

REINER, J. M. **Macromolecular Syntheses in Cell-Free Preparations of** *Escherichia coli*. *J. Bacteriology*. 1960, Feb., v. 79, No. 2, 157–65. [28 refs.]

REINER, J. M. **Macromolecular Syntheses in Cell-Free Preparations from** *Escherichia coli*. *J. Bacteriology*. 1960, Feb., v. 79, No. 2, 166–74. [42 refs.]

MANS, R. J. & KOCH, A. L. **Metabolism of Adenosine and Deoxyadenosine by Growing Cultures of** *Escherichia coli*. *J. Biol. Chem.* 1960, Feb., v. 235, No. 2, 450–56, 2 figs. [24 refs.]

COHN, M., LENNOX, E. & SPIEGELMAN, S. **On the Behaviour of the** *E. coli* **P_2-"β-Galactoside System" introduced into** *Shigella dysenteriae*. *Biochim. et Biophys. Acta.* 1960, Apr. 8, v. 39, No. 2, 255–66, 1 fig. [24 refs.]

JONSEN, J., LALAND, S. & STRAND, Å. **Adaptatio** *E. coli* **to 2-Deoxy D-Ribose.** *Acta Path Microb. Scandinavica.* 1959, v. 47, No. 1, 7 3 figs.

OKAGAKI, H. **Effect of Chloramphenicol on the S vival of** *Escherichia coli* **irradiated with Ul violet Light.** *J. Bacteriology.* 1960, Feb., v. No. 2, 277–91, 15 figs. [18 refs.]

COETZEE, J. N. & SACKS, T. G. **Intrastrain Transd tion in** *Proteus mirabilis*. [Correspondei *Nature.* 1960, Mar. 19, v. 185, 869–70. [13 re

RAMSEY, Carolyn H., HEYL, J. G. & EDWARDS, P. **Three New Arizona Types isolated from Nor Reptiles (5:29:30; 16:22:34; and 20:29:** *Antonie van Leeuwenhoek: J. Microbiol. & Se* 1960, v. 26, No. 1, 47–8.

FINKELSTEIN, R. A. & LABREC, E. H. **Rapid Iden cation of Cholera Vibrios with Fluorescent A body.** *J. Bacteriology.* 1959, Dec., v. 78, No 886–91. [15 refs.]

[An abstract of this paper appeared in the *Trop Diseases Bulletin,* 1960, v. 57, 704.]

JENKIN, C. R. & ROWLEY, D. **The Importance Antibody in the Prevention of Experimen Cholera in Rabbits.** *Brit. J. Exper. Path.* 19 Feb., v. 41, No. 1, 24–30. [17 refs.]

[An abstract of this paper appeared in the *Trop Diseases Bulletin,* 1960, v. 57, 704.]

RICHARDSON, M. **Parasitization** *in vitro* **of Bov Cells by** *Brucella abortus*. *J. Bacteriology.* 19 Dec., v. 78, No. 6, 769–77, 12 figs. [20 refs.]

This is an account of the bovine tissue-culture *Brucella abortus*. The fixed-tissue cells employed w from foetal skin and kidney and from adult ute mucosa, testes, spleen, bone marrow and lung. The c were grown as a monolayer on glass; after 5–10 d growth the cells were exposed to a suspension of cellae in a concentration of 10^2-10^6 bacterial cells culture tube. After incubating at 37°C. for 3–24 ho the brucella-containing medium was removed and placed with fresh tissue-culture medium contai μgm. per ml. streptomycin; this was changed every days. Throughout the period of exposure and intrac lar growth 5% CO_2-in-air was maintained.

H. J. Benst

LAMANNA, C. & EISLER, D. **Comparative Study of Agglutinogens of the Endospores of** *Bac anthracis* **and** *Bacillus cereus*. *J. Bacteriol* 1960, Mar., v. 79. No. 3, 435–41. [11 refs.]

EDINEC, A. A. & MATZKE, H. A. **The Relationship of Toxin and Antitoxin Injection Site to Tetanus Development in the Rat.** *J. Exper. Med.* 1959, Dec. 1, v. 110, No. 6, 1023–40, 2 figs. [38 refs.]

In order to study the conducting path of tetanus toxin o the central nervous system, 3 MLD of the toxin was njected into a number of different sites in the rat—the ein, muscle, endoneurium, epineurium, spinal cord, sub-rachnoid space and the sub-dural space. In addition to his series of experiments, other rats, all of whom had eceived intramuscular injections of tetanus toxin were iven injections of antitoxin (3 minimum protective doses) few minutes later into the sites listed above for the first eries of experiments.

Local tetanus followed the intramuscular and endo-eural injection of toxin. Epineural injections led to both ocal and blood-borne tetanus. Intraspinal injections gave ise to severe tetanus within 4-8 hours with exaggerated yper-sensitivity. Death occurred within 12-25 hours, vith general convulsions just before death. Sub-dural njections were followed by both "dorsal" and blood-orne tetanus. Dorsal tetanus declared itself as a board-ike stiffness of the axial musculature. Intravenous and ub-arachnoid injections resulted in blood-borne tetanus nly. Antitoxin, whatever the site of injection, failed to revent local tetanus from the intramuscular injection of oxin but intramuscular injection of antitoxin regularly revented death and proved to be the most successful of ll injection methods. The authors' experimental results re in general agreement with the conclusions of Payling WRIGHT [this *Bulletin*, 1953, v. 28, 1101; *Guy's Hosp. Rep.* 1956, v. 105, 57] and suggest that the endoneural issue spaces serve as a conduit for tetanus toxin from the nuscle to the central nervous system, the perilemma of he peripheral nerve trunk possibly acting as a selectively ermeable membrane which permits the toxin to pass rom the epineurium to the endoneurium.

H. J. Bensted

MILLER, Pauline A., GRAY, C. T. & EATON, M. D. **Formation and Action of a Peptidase which Hydrolyzes Histidine Peptides required in Tetanus Toxin Synthesis.** *J. Bacteriology.* 1960, Jan., v. 79, No. 1, 95–102, 3 figs. [10 refs.]

D'ARCA SIMONETTI, A. Ricerca *in vitro* della tossinogenesi del *Cl. tetani* e del *Cl. botulinum.* [**Researches on the *in vitro* Demonstration of Toxin Production by *Cl. tetani* and *Cl. botulinum***] *Nuovi Ann. d'Igiene e Microbiol.* 1959, July–Aug., v. 10, No. 4, 342–58, 4 figs. English summary.

The possibilities of application of a gel diffusion test similar to that used by ELEK and others for the detection of diphtheria toxin are discussed.

The most satisfactory method has proved to be to allow the antitoxin to diffuse from cups in the vicinity of a growth of the anaerobe which takes place beneath a glass strip placed centrally on the surface of a plate of liver extract agar [this *Bulletin*, 1955, v. 30, 443].

This method shows marked contrasts between different strains in respect of speed of appearance and density of the lines of precipitate formed. *Cl. tetani* and *Cl. botulinum* type A were the anaerobes tested and gave satisfactory results.

J. W. McLeod

CARDELLA, M. A., DUFF, J. T., WINGFIELD, B. H. & GOTTFRIED, C. **Studies on Immunity to Toxins of *Clostridium botulinum*. VI. Purification and Detoxification of Type D Toxin and the Immunological Response to Toxoid.** *J. Bacteriology.* 1960, Mar., v. 79, No. 3, 372–8, 2 figs. [17 refs.]

HOWES, E. L., MANDL, Ines & ZAFFUTO, S. **Toxicity of Enzymes from *Clostridium histolyticum*.** *J. Bacteriology.* 1960, Feb., v. 79, No. 2, 191–7, 1 fig.

DYMOWSKA, Zofia. Właściwości antygenowe niektórych szczepów leptospir wyosobnionych w Polsce. [**Antigenic Properties of some Leptospira Strains isolated in Poland**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 1, 71–94. [46 refs.] English summary.

BACTERIOPHAGES

BRUMFITT, W. **Studies on the Mechanism of Adsorption and Penetration by Bacteriophage.** *J. Path. & Bact.* 1960, Jan., v. 79, No. 1, 1–9, 3 figs. [34 refs.]

The work described in this paper suggests that the receptors of *Micrococcus lysodeikticus* for phage N_4 are he same as the lysozyme substrate and that an enzyme eleased by freezing and thawing concentrated suspen-ions of phage is a lysozyme.

2 mutants derived from *M. lysodeikticus* LS were used. Mutant LPR selected for phage resistance, was, like its parent, still sensitive to lysozyme. Mutant LR_1, selected for resistance to lysozyme, was also resistant to the phage. LS cell walls acted on by lysozyme no longer adsorbed phage, indicating that lysozyme had destroyed the phage receptors. Mutant LR_1 had been previously shown to be resistant to lysozyme because hydroxyl groups in the cell wall are acetylated [BRUMFITT *et al.*, this *Bulletin*, 1959, v. 34, 156]. Deacetylation was found to

render cell walls of LR_1 sensitive, not only to lysozyme, but also the phage enzyme. On the other hand, acetylation of the cell walls of the strains LS and LPR made them resistant to the action of the phage enzyme.

There were differences in the phage resistance of the 2 mutants. Strain LPR did not adsorb phage, presumably because it had no receptors, but its cell walls were lysed by the free phage enzyme. On the other hand, strain LR_1 did adsorb phage, but it seems the phage could not penetrate the cell walls. Whole phage did not lyse LS cell walls, although free enzyme did, perhaps because the enzyme was confined within the particle.

For the following reasons the enzyme released from the phage is thought to be a lysozyme. Its physical properties were similar to egg white lysozyme. Acetylation of cell walls produced changes in resistance to both enzymes. Lysis of cell walls by both enzymes was accompanied by the release of hexosamine end-groups. Both enzymes lysed *Bacillus megatherium* and neither lysed *Staphylococcus aureus*.

This system differs in several respects from the T2 system, but this is not surprising since T2 receptors are situated in the lipo-protein layer of the *Escherichia coli* B cell wall (Weidel, *Ann.Rev. Microbiol.*, 1958, v. 12, 27) while *M. lysodeikticus* cell walls contain little or no lipid (Salton, *Biochim. et Biophys. Acta.*, 1953, v. 10, 512). Chemical blocking of carboxyl, amino and sulphydryl groups in the cell surface did not prevent uptake of phage N_4, though it blocks T2 adsorption. Also it has been suggested that T2 penetration follows activation of an enzyme in the cell wall by the attachment of the phage [Puck and Lee, this *Bulletin*, 1955, v. 30, 432]. Heating cell walls of *M. lysodeikticus* to 100°C. did not modify the action of the phage enzyme.

Janice Taverne

Boyd, J. S. K. & Bidwell, D. E. **The Q1 (A) Strains of *Salmonella typhimurium*: Induction Phenomena.** *J. General Microbiol.* 1959, Dec., v. 21, No. 3, 635–51, 10 figs. [16 refs.]

12 strains of *Salmonella typhi-murium* Q1, each lysogenic with a different type A phage, were irradiated with UV light and their behaviour investigated. At most 40% of the bacteria were induced. Phage was liberated about 45 minutes, after irradiation, but the burst size varied considerably and the cultures showed different degrees of clearing. 2 strains were investigated in greater detail. After irradiation, they both produced the same amount of free phage but cultures lysogenic with phage A1c showed no clearing while cultures lysogenic with the closely related phage A1b showed well-marked clearing. No evidence of a lysin capable of causing the clearing could be obtained, and the proportion of cells being induced was the same in both cases. Observations on morphology and viable counts, and comparison with the reaction to irradiation of the non-lysogenic Q1 strain, suggested that clearing was related to the particular bacteria which were being induced rather than to the total number. With A1c, induction occurred in the cells which would have received a lethal dose of irradiation, so the more lightly irradiated bacteria were free to grow up and mask the lysis of the induced bacteria. With A1b, induction occurred in the cells which would otherw have survived irradiation, so the culture cleared.

Thus although the same host was concerned in bo cases and UV light is thought to cause induction by action on the host [Jacob, this *Bulletin*, 1955, v. 30, 65 the 2 prophages each have their own specific triggeri mechanism. Prophages A1b appears to be activated a hit which is less lethal to the host cell than the which activates prophage A1c. *Janice Taverne*

Brandis, H. Über die Verschiebung der Lysosensibili bei *S. java-* und *S. paratyphi B*-Stämmen dur Prophagensubstitution. [**Alteration of Lysosen tivity in Strains of Salmonella *Java* and *Sal paratyphi B* by Prophage Substitution**] *Ztschr. Hyg. u. Infektionskr.* 1959, v. 146, No. 1, 66– [13 refs.]

Strain No. 1066 of Salmonella Java grown in bro liberated a temperate phage (P6) which could be detect by using strain No. 231 of Salm. Java as the indicat organism. Strain No. 1118 similarly liberated the te perate phage P8. On strain No. 1118 P6 phage form plaques which were scarcely visible to the naked eye a multiplied to a titre of $2{\cdot}5 \times 10^9$ per cc.; P8 form larger plaques and gave a somewhat lower titre ($2{\cdot}8$ 10^8). The 2 phages showed an antigenic relationship cross-neutralization tests, but had different ranges activity against a series of strains of Salm. Java. T 2 strains of Salm. Java from which the phages had be isolated were each susceptible to lysis by the heterologo phage but could easily be lysogenized by it as a result prophage substitution. The lysogenization could also reversed, thus restoring the original properties of t strains. The type strain No. 228 of *Salm. paratyphi* of lysotype 2 could be lysogenized by P8 phage with t production of some colonies of lysotype 1, which had al thereby acquired sensitivity to P6 phage. The lysoge zation with P8 phage also displaced the characteris prophage of *Salm. paratyphi B* type 2 and strains th affected acquired susceptibility to lysis by the 1, Jers 3a and 3aI test phages. *D. J. Baue*

Husmann, K. H. Experimenteller Beitrag zum Proble der Inaktivierung von Bakteriophagen durch d Properdin-System. [**An Experimental Contrib tion to the Problem of the Inactivation of Phag by the Properdin System**] *Ztschr. f. Hyg. u. Infe tionskr.* 1959, v. 146, No. 1, 89–96, 2 figs. [refs.]

The author has investigated the neutralization of t T2r+ phage of *Escherichia coli* by properdin, a reacti which is the basis of the method of titrating prop din proposed by Barlow *et al.* [see this *Bullet* 1958, v. 33, 992 *bis*; *Proc. Nat. Acad. Sci.*, 1956, 42, 391]. Pooled human, guineapig, mouse and rat s in dilutions ranging from 1:2 to 1:16 were mixed w $0{\cdot}1$ cc. of a phage preparation containing $7{\cdot}5 \times 10^5$ p ticles and then plated, and the dilution of serum wh inactivated 50% of the phage particles was calcula from counts of the plaques obtained. In experime

with 15 samples of pooled sera it was found that the initial inactivation titres of the fresh sera fell by 16·7–100% after storage for 10 days at −20°C. A similar fall was observed in a further experiment in which 10 replicate titrations were carried out on pooled serum from 10 rats before and after storage for 8 days at −20°C. Studies of the rate of inactivation carried out with pooled guineapig sera showed that the minimum titre was attained after 5 days or so. A fall in titre has not been observed in titrations of properdin by the zymosan method [this *Bulletin*, 1955, v. 30, 83] and the results therefore suggest that some substance other than properdin is being determined by the phage neutralization test. *D. J. Bauer*

MUTSAARS, W. La réactivation multiple du bactériophage inactivé par voie physique et chimique. Quatrième partie. **[Multiplicity Reactivation of Bacteriophage inactivated by Physical and Chemical Agents]** *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 119–30. [16 refs.]

When phage ϕN was inactivated by treatment with 0·3% glyoxal for 1 hour at 37°C. and then mixed with *Escherichia coli* W at different multiplicities, more phage was recovered at the higher multiplicity. Multiplicity reactivation was also demonstrated with phage which had been deaminated by sodium nitrite, and when phage inactivated by either method was mixed with phage inactivated by UV irradiation.

Experiments on the inactivation of plant and animal viruses by glyoxal suggest that, like formalin, it acts by combining with nucleic acids (*e.g.*, STAEHELIN, *Biochim. Biophys. Acta*, 1959, v. 31, 448). There were, however, some points of difference between glyoxal and formalin. With phage N, but not with influenza virus, formalin was more active than glyoxal. Both formolized phage and deaminated phage, in conditions of single infection, gave more plaques when adsorption took place at 0°C. and the plates were held at 42°C. for 1½ hours before overnight incubation at 37°C., but this was not true of phage treated with glyoxal. *Janice Taverne*

FRY, B. A. **Conditions for the Infection of *Escherichia coli* with Lambda Phage and for the Establishment of Lysogeny.** *J. General Microbiol.* 1959, Dec., v. 21, No. 3, 676–84, 3 figs.

Upon infection with λ_{22} phage, the proportion of *Escherichia coli* K112 cells becoming lysogenic increased, while that of refractory cells decreased, with the concentration of $MgSO_4$ in the adsorption medium. At low concentrations as many cells gave the lytic response as the lysogenic response, but in the optimum conditions of 0·02M $MgSO_4$ at *p*H6·6 when 99% of the cells were infected, over 90% were lysogenized. The rate of adsorption of phage was also fastest in the presence of 0·02M $MgSO_4$ and the number of phage particles adsorbing per cell was greatest. Although increasing multiplicity caused an increase in the number of cells becoming lysogenic, as it does for *Salmonella typhi-murium* [BOYD, this *Bulletin*, 1951, v. 26, 1111], there is some evidence that the effect of $MgSO_4$ was not only to give better adsorption and therefore higher multiplicities, but to favour the lysogenic pathway at another level, perhaps by playing a part in the attachment of the prophage to the bacterial genome.

Experiments in which bacteria were irradiated with UV light before infection showed that the capacity to give the lysogenic response was lost before the colony forming ability and that after doses which destroyed the colony forming ability the cells could still produce phage, *i.e.*, give the lytic response. *Janice Taverne*

FRY, B. A. & GROS, F. **The Metabolic Activities of *Escherichia coli* during the Establishment of Lysogeny.** *J. General Microbiol.* 1959, Dec., v. 21, No. 3, 685–92, 5 figs. [23 refs.]

A culture of *Escherichia coli* K112 was infected with λ_{22} in conditions in which 91% of the cells became lysogenic [see above] and, from the moment of suspension in broth, the metabolic activities of the cells compared with those of an uninfected control culture. The lag period before growth began (measured by turbidity and viable counts) was over 3 times longer in the infected culture than in the control. Synthesis of the induced enzyme β-galactosidase began after 40 minutes in the control and not at all during the course of the experiment in the cells being lysogenized. Other protein synthesis, measured by the incorporation into cell protein of ^{14}C from labelled DL-phenylalanine in the growth medium, resumed immediately in the control but not for 120 minutes in the infected culture. Similarly, both RNA and DNA synthesis began at once in the control but not for 120–140 minutes in the infected culture.

It appears, then, that in the cell being lysogenized the net synthesis of proteins and nucleic acids in the host cell is blocked and there is a delay in cell division. That the prophage becomes attached to the bacterial genome in a cell in which most of the synthetic activities have temporarily stopped is consistent with the findings that factors which reduce cell metabolic activities, such as a drop in temperature [BERTANI and NICE, this *Bulletin*, 1955, v. 30, 162] or chloramphenicol (CHRISTENSEN, *Virology*, 1957, v. 4, 184), favour lysogeny.

Janice Taverne

LOEB, T. **Isolation of a Bacteriophage Specific for the F+ and Hfr Mating Types of *Escherichia coli* K-12.** *Science.* 1960, Mar. 25, v. 131, 932–3.

THOMPSON, Norah. **The Influence of Acidity on the Multiplication of Lactic Streptococcal Bacteriophage in Liquid Media.** *J. Applied Bact.* 1959, Aug., v. 22, No. 2, 287–93, 2 figs. [10 refs.]

BERTANI, G. **Sensitivities of Different Bacteriophage Species to Ionizing Radiations.** *J. Bacteriology.* 1960, Mar., v. 79, No. 3, 387–93, 1 fig. [51 refs.]

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

RHODES, A. J. **Recent Advances in Virus Infections: the New Era in Virology.** *Brit. Med. J.* 1960, Apr. 9, 1071–7. [Numerous refs.]

20 years ago only 36 human viruses were recognized and only 22 could be reliably propagated in the laboratory; now 152 pathogenic human viruses are recognized and only 5 important viruses cannot be propagated. The major techniques responsible for this advance have been the use of suckling mice and tissue culture. The effects of a virus on cells in culture may be merely destructive, or recognizable lesions such as the inclusions of measles may be demonstrated. Tissue cultures have also made possible the manufacture of vaccines, notably for poliomyelitis. Laboratory diagnosis is concentrating more on the isolation and identification of viruses than, as previously, mainly on serology. The enteroviruses which comprise polioviruses, Coxsackie and ECHO viruses have many similar physical and chemical properties, their modes of spread and their pathogenesis are also similar, and paralysis, aseptic meningitis and summer fever may be caused by members of all 3 groups, rubelliform rashes by all except poliovirus. Newer respiratory viruses include the adenoviruses and several other groups. The adenoviruses occur in 20 types but the commonest symptoms are pharyngitis, fever and keratoconjunctivitis. The arborviruses are now a large group which can be divided into at least 3 antigenic groups—many of them are known to infect man and cause disease.

C. E. Gordon Smith

TAMM, I.; NEMES, Marjorie M.; OSTERHOUT, S.; BABLANIAN, R. **On the Role of Ribonucleic Acid in Animal Virus Synthesis. I. Studies with 5,6-Dichloro - 1 - β - D - Ribofuranosylbenzimidazole** [TAMM, NEMES & OSTERHOUT]. *J. Exper. Med.* 1960, Mar. 1, v. 111, No. 3, 339–49. [21 refs.] **II. Studies with Ribonuclease** [TAMM & BABLANIAN]. *Ibid.*, 351–68, 5 figs. [23 refs.]

I. "Adenosine, but not guanosine, was capable of blocking the inhibitory effect of 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole (DRB) on influenza virus multiplication in the chorioallantoic membrane *in vitro*. At virus inhibitory concentrations DRB caused marked inhibition in uptake of adenosine-8-C^{14} into RNA of uninfected host cells, but it had little effect on uptake of C^{14}-L-alanine into host cell proteins or on cellular oxygen consumption. The activity of DRB in inhibiting multiplication of the DNA-containing adenovirus was similar to its inhibitory activity on multiplication of the RNA-containing influenza virus. These and earlier results are discussed from the point of view of the important role of RNA in the reproduction of DNA-containing viruses."

II. "Ribonuclease is a highly active inhibitor of vaccin virus multiplication *in vitro* in the chorioallantoic mem brane removed from embryonated chicken eggs. It also a highly active inhibitor of pock formation by va cinia and herpes simplex viruses on the chorioallanto membrane *in vivo*. Marked inhibitory effects we obtained with 12.5 μg. of RNase. However, comple inhibition was not obtained with several hundred micr grams of the enzyme.

"RNase caused no inactivation of the infectivity vaccinia virus particles but it had a marked inhibito effect on multiplication of this virus when administere many hours after infection of host cells had occurre RNase also failed to inactivate the infectivity of herp simplex virus particles.

"The results obtained indicate that ribonucleic acid necessary for the multiplication of two DNA-containir viruses; *i.e.*, vaccinia and herpes simplex."

WEINSTEIN, L. & CHANG, Te-Wen. **The Effect Colchicine and some Chemically Related Com pounds on Experimental Viral Infections.** *Ant biotics & Chemotherapy*. New York. 1960, Ma v. 10, No. 3, 180–87, 3 figs.

"1. Colchicine, colchiceine, isocolchicine, animoco chicide, butylaminocolchicide, and propylaminocolch cide given to mice prior to infection with influenza encephalomyocarditis virus, produced a mild degree slowing of the rate of death but did not reduce the tot number of fatalities.

"2. The study of colchicine and its closely related der vatives is complicated by the high degree of toxicity these compounds.

"3. Acetylcolchinol, colchinol methyl ether ditartrat N-acetyl colchinol methyl ether, dihydrodeamino co chinol methyl ether, N-acetyl isocolchinol, 5-amino dibe (1,3) (a,c)-cycloheptadiene hydrochloride, dibenz (1, (a,c)-cycloheptadien-5-one, and 10-N-acetylamino-2,3,4, tetramethoxyphenanthrene have been found to alter t course of encephalomyocarditis infection in mice. Son of these agents were active only either prophylactically therapeutically. Most of them were effective when the administration was instituted two days before or one two days after initiation of infection.

"4. The most remarkable effect of the active deriv tives of acetylcolchinol was slowing of the death ra With some compounds, a reduction of the total numb of deaths to 50% of that in the controls was observe

"5. In the doses used, 10-amino-2,3,4,7-tetramethox phenanthrene and 9-amino-2,3,4,7-tetramethoxyphena threne had no effect on the course of encephalomyoca ditis infection in mice when administered either prior or after injection of the infectious agent."

NEUSTROEV, V. D., KHANDUEV, T. T. & MILIUTIN, V. N. **The Use of Fluorescence Microscopy for demonstrating Ornithosis Virus in the Organs of Infected Animals.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 358–61, 3 figs. [Translated from Russian.]

Ornithosis virus can be demonstrated in smear by fluorescent microscopy. Acridine orange in a 1 in 30,000 aqueous solution proved the most suitable dye.

S. P. Bedson

IAKOVLEV, A. I., KHANDUEV, T. T. & KLEPUKOV, A. A. **Micro-Agglutination Test with Rickettsias and Viruses by means of the Fluorescence Microscope.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 398–402, 2 figs. [Translated from Russian.]

With suspensions of *Rickettsia burneti* and *R. prowazeki* containing 10^9 rickettsiae per ml., specific micro-agglutination was demonstrated on the slide (a drop each of rickettsial suspension, serum dilution and a 1 in 10,000 dilution of fluorochrome) by means of the fluorescent microscope. Comparison of this test with the complement-fixation test showed a close correlation.

An antigen was made from ornithosis virus grown in the yolk sac of the chick embryo, inactivated by 0·4% phenol or 0·2% formalin, purified by fractional centrifugation after treatment for 72 hours at 4°C. with 1 in 1,000 $KMnO_4$ and 1 in 500 H_2O_2 and concentrated to a turbidity equivalent to that of a bacterial suspension of 10^9 bacteria per ml. With the fluorescent micro-agglutination technique specific agglutination was obtained with this antigen and the use of this reaction for the detection of ornithotic antibody in the sera of infected birds and animals demonstrated.

S. P. Bedson

MASON, D. M. **A Capillary Tube Agglutination Test for detecting Antibodies against Ornithosis in Turkey Serum.** *J. Immunology.* 1959, Dec., v. 83, No. 6, 661–6.

The antigen used in this capillary agglutination test (CTA) was prepared from a virulent strain of ornithosis virus grown in the allantoic cavity of the chick embryo. The fluid was inactivated by formalin (1%; 24 hours at 37°C. and 24 hours at room temperature) and the virus was then centrifuged out, washed and resuspended to 10 times its concentration in the infected fluids; it was then stained by Giemsa. After several washings the elementary bodies were suspended to 20 times the concentration in the original allantoic fluid. Falling serum dilutions were mixed with the suspension of stained virus in glass capillaries (0·4 mm. diameter) which were stood vertically in plasticine and read by naked eye after 4 hours at room temperature and again after standing overnight. This test was applied in parallel with the indirect (ICF) and direct complement-fixation (DCF) tests on the sera of artificially and naturally infected turkeys and a lesser number from inoculated parrots and from pigeons in infected flocks. There was a close parallelism between the results obtained with the CTA and the ICF, both of which were more delicate than the DCF. Some false positives were noted in the CTA with the lower serum dilutions but a positive at a dilution of 1 in 16 constituted presumptive evidence of infection.

S. P. Bedson

PORTERFIELD, J. S. & ALLISON, A. C. **Studies with Poxviruses by an Improved Plaque Technique.** *Virology.* New York. 1960, Feb., v. 10, No. 2, 233–44, 2 figs. [13 refs.]

Plaques formed by vaccinia virus on monolayers of chick embryo fibroblasts were larger, appeared earlier, and were more numerous when the agar overlayer was buffered with tris(hydroxymethyl)aminomethane than with bicarbonate. The same titre was obtained with the adsorption medium held at different *p*H's within the range *p*H 6·0–7·5. Titres of suspensions of vaccinia, cowpox, ectromelia and herpes simplex viruses obtained from such plaque counts were of the same order as those from pock counts on the chick chorioallantoic membrane. Unlike the other viruses, plaque formation with ectromelia was best when plates were incubated at 35°C., and it was completely suppressed at 39°C. Though the size of plaques formed by the other viruses was reduced at 39°C., their number was not.

Janice Taverne

SOLOV'EV, V. D. & MASTIUKOVA, I. N. **Methods of Titrating Vaccinia and Variola Viruses and Neutralizing Antibodies.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 370–74, 3 figs. [Translated from Russian.]

These authors titrated vaccinia and variola viruses by inoculating cultures of 4 different cell strains and the chorioallantoic membranes of chick embryos, and by intradermal injection of rabbits. Titres of virus in rabbits were taken as the highest dilutions of suspension causing skin infiltration. In the chick embryos and tissue cultures the 50% infectious end point was taken. Infected centres in cell cultures were made more clearly obvious by the adsorption of washed chick red cells. [This method was described recently by DRIESSEN and GREENHAM, this *Bulletin,* 1959, v. 35, 1187, and by VIEUCHANGE, *ibid.,* 1960, v. 35, 401.] Chick embryos and tissue cultures were 100-fold more sensitive than rabbit skin. It was also possible to titrate antivaccinial antibody by inhibition of cytopathic change in tissue cultures; the larger the dose of challenge virus, the lower the titre of neutralizing antibody found.

Colin Kaplan

HANAFUSA, H., HANAFUSA, T. & KAMAHORA, J. **Transformations of Myxoma into Vaccinia or Ectromelia Virus in Tissue Culture.** [Correspondence.] *Nature.* 1959, Oct. 10, v. 184, Suppl. No. 15, 1152–3.

In the presence of heat-inactivated vaccinia or ectromelia viruses, myxoma virus was transformed into infectious vaccinia or ectromelia virus in human amnion

cell cultures. When poliomyelitis and measles viruses were used as the active virus, there was no transformation in the presence of heat-inactivated vaccinia virus. [See Fenner *et al.*, this *Bulletin*, 1959, v. 34, 948.]

Colin Kaplan

Waterson, A. P. **Plaque Formation by Herpes Virus in Chick Embryo Tissue.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 592–9, 4 figs. [12 refs.]

The Melbourne egg- and mouse-adapted variant of the HF strain of herpes virus formed satisfactory plaques on chick embryo monolayers grown in plates. The plaques appeared on the 3rd day of incubation and were most conveniently counted on the 4th day. The method gave titres which were in close agreement with those obtained by pock counting and by determining the TCD50 in chick embryo and rabbit kidney cultures.

D. J. Bauer

Beswick, T. S. L. **Further Observations on Experimental Herpes Simplex Infection in the Baby Mouse.** *J. Path. & Bact.* 1960, Jan., v. 79, No. 1, 69–76.

After passage, either through baby mice, rabbit cornea or chick chorioallantoic membrane, a strain of herpes simplex which originally caused an ascending myelitis and paralysis when inoculated intraperitoneally into suckling mice [this *Bulletin*, 1959, v. 34, 176], no longer caused lesions of the central nervous system but lesions in the organs of the peritoneal cavity instead. The change did not seem to be due to the virus being replaced by or contaminated with another agent since the lesions, which were still typical of herpes, were completely neutralized by herpes antiserum and not affected by antiserum prepared with normal mouse tissue, and no evidence of infection was obtained when a suspension of normal mouse tissue was passed from mouse to mouse. Intracerebral inoculation showed that the virus had not lost the ability to multiply in nervous tissue, and lesions in the spinal cord were observed after subcutaneous inoculation into the intrascapular fat pad. The author suggests that adapted or altered virus inoculated intraperitoneally may not have caused paralysis because the increasing severity of the lesions near the site of injection, and the inflammation and tissue damage there, may have prevented the virus reaching the central nervous system.

Janice Taverne

Hoggan, M. D., Roizman, B. & Turner, T. B. **The Effect of the Temperature of Incubation on the Spread of Herpes Simplex Virus in an Immune Environment in Cell Culture.** *J. Immunology.* 1960, Feb., v. 84, No. 2, 152–9, 3 figs. [17 refs.]

In the presence of herpes antibody a variant of herpes simplex virus produced macroplaques in cultures of human amnion cells (strain FL). In preliminary experiments one infected cell was shown to give rise to one plaque, and one infectious particle was required to infec one cell. When infected cells were plated on monolaye in a medium containing pooled human serum, and th cultures were incubated at various temperatures, th mean plaque area was found to be higher after 4 day incubation at 37°C. than at temperatures above or belov The amount of virus released from the cells was als greater at 37°C. than at higher or lower temperature [Hoggan and Roizman, this *Bulletin*, 1960, v. 35, 612 although the amount of virus formed, and the rate c formation, was greatest at 34°C. As virus does not sprea through the fluid medium in the presence of antibod [*Ibid*, 613] the increase in macroplaque size was take to be a measure of cell to cell transmission. The rat of virus spread does not appear to be related to th amount of virus formed, so much as to the amoun released, and there is evidence that this relationship i not straightforward.

Janice Taverne

Schmidt, B. & Grossgebauer, K. Myxovirus Hämagglutinationsversuche mit unterschiedliche Erythrocytenarten. Vergleichende quantitative Ur tersuchungen unter verschiedenen Bedingunger [**Experiments on the Haemagglutination of Myxo viruses with Different Kinds of Red Cel Comparative Quantitative Investigations unde Different Conditions**] *Ztschr. f. Hyg. u. Infek tionskr.* 1959, v. 146, No. 1, 26–47, 1 fig. [97 refs

The authors have studied the agglutination by strains of influenza virus, and also mumps and Nev castle disease viruses, of chick, guineapig, sheep, bovin horse, pig and cat red cells. Only 4 strains (A/Asia 5 mumps, Lee and B_{1955}) agglutinated all types of red cel all 15 strains agglutinated chick, guineapig and shee red cells, and a number of differences in behaviour wer noted in the remaining tests. Heating at 56°C. for minutes destroyed the haemagglutination of mumps ar Newcastle disease viruses, but had little effect upon th activity of the influenza strains. Differences in behavio during elution were noted; 3 influenza strains would on agglutinate sheep red cells at room temperature aft inactivation, and most strains would only agglutina bovine cells at 4°C. Observations were also made c panhaemagglutination and the zone phenomenon.

D. J. Bauer

Mäkelä, O., Cantell, K. & Penttinen, K. **Failure Mumps Virus to inactivate Agglutinogens M, and Rh_0 (D) of Human Red Cells.** *J. Immun logy.* 1959, Aug., v. 83, No. 2, 127–32, 1 fig. [refs.]

Human red cells were incubated for 3 hours at 37° with the Enders strain of mumps virus in the form of i fected allantoic fluid with a haemagglutinin titre of 6 or as a partially purified preparation with a titre of 51 1024, and after washing in saline the effect of exposu to the virus upon the agglutinogens of the red cells w investigated. The Rh_0 agglutinogen was unaffected a both Rh-positive and Rh-negative red cells retained th original serological behaviour after treatment; it was n

possible to detect Rh_0 agglutinogen in eluates from Rh-positive red cells which had been treated with the virus. These findings are in opposition to those of BIGLEY and co-workers (*J. Immunology*, 1958, v. 80, 85). The treated cells also contained M and N agglutinogens, whereas these were inactivated when the cells were treated with the Lee strain of influenza virus. *D. J. Bauer*

ANANTHANARAYAN, R. & PANIKER, C. K. J. **Non-Specific Inhibitors of Influenza Viruses in Normal Sera.** *Bull. World Health Organization.* Geneva. 1960. v. 22, Nos. 3/4, 409–19. [22 refs.]

The presence of inhibitors of haemagglutination by influenza virus types A, A1, A2, swine and B was tested in normal sera from guineapigs, horses, monkeys, dogs, cows, rabbits, sheep and fowls, and in acute-phase human sera collected during the 1957 pandemic. All sera contained normal inhibitors active against at least some of the virus strains. Removal of inhibitors from each serum by (a) heating at 56°C. for 30 minutes, (b) receptor-destroying enzyme (c) potassium periodate, (d) trypsin and (e) trypsin plus potassium periodate (Alabama method) was investigated. No single procedure was effective in removing inhibitors for all virus strains but the authors feel that a combination of trypsin and potassium periodate offers the best prospects for general application. [It is impossible to abstract the abundant material presented in tabular form in this paper.] *H. G. Pereira*

SPENCE, L. **Kaolin Treatment of Sera for Removal of Nonspecific Inhibitors to Asian Strains of Influenza Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 425–7.

"The use of kaolin for treatment of sera in diagnosis of kaolin treatment over other technics warrant further test is reported. Comparison of kaolin treatment with other methods in common use is made. The advantages of kaolin treatment over other technics warrant further trial of the method."

SZCZYGIELSKA, Jadwiga, PINKIEWICZ, H., BIERNACKI, M. & PLESZCZYNSKA, Ewa. Badania nad patogenzą grypy doświadczalnej u myszy białych. Doniesienie II. [**Studies on the Pathogenesis of Experimental Influenza in White Mice. Report II. Anatomopathological Lesions**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 1, 15–19, 4 figs. on 2 pls.

The English summary appended to the paper is as follows:—

"It was stated that influenza virus introduced experimentally into intestines of white mice caused anatomopathological lesions in lungs, liver and spleen of infected animals. The lesions in lungs showed an interstitial inflammatory character."

DRESCHER, J. Über die Beziehungen zwischen Antigenzufuhr und Antikörperbildung. I. Mitteilung. Beschreibung einer Methodik zur Gewinnung hochtitriger Immunseren mittels Antigendauerreizen. [**The Correlation between Antigen Supply and Antibody Production. I. A Method for the Production of Highly Potent Immune Sera by Permanent Antigenic Stimulation**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 149–60, 1 fig.

Permanent antigenic stimulation was produced in guineapigs by the repeated intraperitoneal injection of purified influenza virus in a volume of phosphate buffer which was too great to be completely absorbed between one injection and the next. The amount of virus absorbed was determined from an examination of the residual fluid. The titres of inhibiting antibody which were obtained by this method over a period of 30 days were much higher than those obtained with a single injection of the same amounts of antigen given each day over the same period. The method of permanent antigenic stimulation also gave high titres of inhibiting antibody in chickens and ferrets *D. J. Bauer*

KILBOURNE, E. D. & MURPHY, J. S. **Genetic Studies of Influenza Viruses. I. Viral Morphology and Growth Capacity as Exchangeable Genetic Traits. Rapid *in Ovo* Adaptation of Early Passage Asian Strain Isolates by Combination with PR8.** *J. Exper. Med.* 1960, Mar. 1, v. 111, No. 3, 387–406, 1 text fig. + 4 figs. on 4 pls. [21 refs.]

Propagation of A2 (Asian) influenza virus in the allantoic cavity of fertile eggs inoculated 1 hour previously with a large dose of inactivated A (PR8) virus resulted in the emergence of recombinant forms. Some recombinants were characterized by A2 antigenicity and A (spherical) morphology whereas in others the A antigenic character was associated with filamentous morphology. Change from filamentous to spherical morphology coincided with increased growth rate and high virus yields.

It is suggested that this procedure may be of value for the "adaptation" of new virus isolates to grow in eggs and the possible application of these findings to the rapid development of efficient vaccines against new virus strains is discussed. Failure of previous attempts to obtain recombinant forms of Asian strains with increased growth capacity is explained mainly by the fact that such attempts had been made with inactivated Asian and infective PR8 strains in which case the chances of recombinant forms out-growing the infective parent strain are reduced. *H. G. Pereira*

LANGE, F. C. Über die toxische und antigene Wirksamkeit von Viren. II. Mitteilung: Qualitative Untersuchungen über die Bildung und Messung haemagglutinationshemmender Antikörper. [**The Toxic and Antigenic Efficacy of Viruses. II. Communication: Qualitative Investigations of Formation and Measurement of Haemagglutination Inhibiting Antibodies**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 488–504, 3 figs. [18 refs.]

The English summary appended to the paper is as follows:—

"As the judgment concerning the demonstrations of a specific formation of hemagglutination inhibiting antibodies is frequently made difficult by inspecific influences, the turnover relation of influenza viruses with hemagglutination inhibiting substances of the serum samples taken on different days was examined during experimental antigen addition. An influenza virus strain of the subtype A_2 was used, which was sensitive in the hemagglutination inhibiting test to inspecific serum inhibitors. The turnover relation with specific antibodies was determined by the equation of Freundlichs Adsorption isotherm, the constant of which could, after a certain period of antigen addition be determined as specifically characteristic. By exact calculation of the specific equation of reaction it became possible to find the qualitative transition from unspecific to specific antigen-antibody reactions and to determine its time values approximately. The experiments and their system is described in detail, the evaluation of the results is discussed."

ROMANOWSKA, Elżbieta. **Studies on Blood Group Antigens M and N. IV. Action of Influenza Virus Enzyme on the Blood Group Substances M and N.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 4, 749–57, 4 figs. on 2 pls. [19 refs.] **V. The M and N Blood Group Substances as Inhibitors of Influenza Virus Haemagglutination.** *Ibid.*, 759–64. [11 refs.]

IV. "The influenza virus (strain Lee) was incubated at 37°C. with water soluble M- or N-blood group substances prepared from human erythrocyte stroma. The action of virus has resulted in loss of serological specificity of the active material concomitant with the release of sialic acid (N-acetylneuraminic acid). After release of about 50% of sialic acid content M- and N-substances have no serological activities. The maximal quantity of sialic acid liberated from the substance with influenza virus enzyme amounted to about 80%."

V. "It was found that M- and N-blood group substances from human erythrocytes are inhibitors of influenza virus haemagglutination. The inhibitory concentration of these substances were determined on the influenza virus strains Lee and PR8.

"About 0·02 μg of M- or N-preparation inhibits 1 haemagglutinating unit of indicator virus Lee.

"0·05–0·1 μg of M- or N-preparation inhibits 1 haemagglutinating unit of indicator virus PR8.

"The M- or N-substance that lost about 50% of its original sialic acid after incubation with virus Lee at 37°C. reveals the almost complete deficiency of inhibiting properties for the strain PR8 and it decreases these properties about 40–60-fold for the strain Lee."

GROSS, W. O. Zur Influenzavakzine-Züchtung. [**Cultivation of Influenza Vaccine**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 632–5, 1 fig.

Influenza B virus was carried through 4 allantoic passages in 2 parallel series of fertile eggs in the presence of immune serum. The eggs of one series were irradia with X-rays at a dose of 1000r 45 minutes after inf tion and the other series served as a control. Passa were made with allantoic fluids which contained virus spite of the presence of antibody. These were found m frequently in the irradiated series, and after 4 passa the neutralization titre with influenza B antiserum virus from irradiated eggs was lower (512) than that virus from the control series (2000), and the titres both were lower than the initial value (8000). The resu are ascribed to mutation, which was presumably high under the influence of irradiation. *D. J. Baue*

HOSAKA, Y. **On the Hemolytic Activity of HV I. An Analysis of the Hemolytic Reactio** *Biken's J.* Osaka. 1958, Nov., v. 1, No. 1, 70–8 14 figs. [24 refs.] **II. Decrease of Sphingomyel in Red Blood Cells hemolysed by HVJ.** *Ibi* 90–99, 6 figs. [14 refs.]

I. "The hemolytic activity of HVJ (Sendai virus) w found to be enhanced in various ways. Centrifugal fra tionation showed that the enhanced activity was s combined with virus particles and isolation of free hem lysin was not successful. A comparison of several pr perties showed the "enhanced" hemolytic activity is n essentially different from that of original virus.

"The hemolytic process in this virus was a first ord reaction and the hemolytic activity was quite differe from the hemagglutinating or eluting activity.

"In the hemolytic reaction, an initial and a later sta could be differentiated when the hemolysis developed low temperature or in the presence of antiserum. A though the hemolytic activity of HVJ is like that lecithinase in some properties, its true nature seems to different."

II. "Paper chromatography of the phospholipids e tracted from red cells hemolysed by virus showed decrease in concentration of sphingomyelin as compare to that in the control. Further by quantitative chemic analysis a decrease of sphingomyelin in the viru hemolysed red cells was shown. This decrease was n caused by liberation of sphingomyelin from the cell but by a decomposition of the substance. As lecith and cephalin are concerned any change was not ab to be detected. This change in the cells seems to l correlated only with the hemolytic activity of the virus

TADOKORO, J. **Modified Virus Particles in Undilute Passages of HVJ. I. The Production of Modifie Particles.** *Biken's J.* Osaka. 1958, Dec., v. No. 2, 111–17, 3 figs. [18 refs.] **II. The Chara teristics of Modified Particles.** *Ibid.*, 118–28, 1 figs. (6 on 3 pls.) [16 refs.]

I. "The accumulative growth curves of HVJ (Send virus) (Z strain) were studied *in ovo*. Growth curves r presented difference in inoculum size, *e.g.*, the larger th inoculum used, the shorter the time required to reach th maximal virus yield.

"Undiluted passages were continued through the 20th transfer with 24 hours and 36 hours incubation periods. In these experiments, the I/A ratio was approximately 10^6 and did not decrease to less than 10^5.

"However, the virus yields obtained in later undiluted passages were less than those of earlier undiluted or standard passages. The hemolytic activity of the virus produced in later undiluted passages was less than that in standard passages."

II. "Further results on the characteristics of HVJ Z strain, propagated in undiluted passages were compared with those of virus particles in standard passages. Particles produced in later undiluted passages had a lower sedimentation constant and were more fragile than those in standard passages or in earlier undiluted passages. Hemagglutinating activity of particles in later undiluted passages was more labile to heating to 45°C. than that in standard passages.

"Susceptibility to inactivation by freeze-thawing changed greatly in later undiluted passages. The hemolytic activity of particles in later undiluted passages was lower than in standard passages, and like that of particles in standard passages was increased by freeze-thawing."

BAKOS, K. & DINTER, Z. **Identification of a Bovine Mucosal-Disease Virus isolated in Sweden as *Myxovirus para-influenzae 3*.** [Correspondence.] *Nature.* 1960, Feb. 20, v. 185, 549–50.

A cytopathic agent identified as *Myxovirus para-influenzae* 3 [see ANDREWES *et al.*, this *Bulletin*, 1959, v. 34, 1056] was isolated from nasal and tracheal exudate of cattle suffering from bovine mucosal disease in 2 of 9 herds investigated in northern Sweden. [See also ABINANTI and HUEBNER, *ibid.*, 1960, v. 35, 90.]

H. G. Pereira

JACKSON, G. G., DOWLING, H. F. & MOGABGAB, W. J. **Infectivity and Interrelationships of 2060 and JH Viruses in Volunteers.** *J. Lab. & Clin. Med.* 1960, Mar., v. 55, No. 3, 331–41, 3 figs.

The role of 2060 [PELON *et al.*, this *Bulletin*, 1957, v. 32, 629] and JH (PRICE, *Proc. Nat. Acad. Sci.*, 1956, v. 42, 892) viruses in the aetiology of upper respiratory infections was tested by intranasal administration of tissue culture virus passages to 159 young adult volunteers. Uninfected tissue culture materials or buffered saline solution were administered by the same route to 96 volunteers observed under the same conditions as controls. The volunteers were not isolated from the general population. Clinical symptoms consistent with a diagnosis of common cold developed after a period of incubation of less than 24 hours in 25 (28%) of 90 volunteers given 2060 virus and in 9 (16%) of 56 concurrent controls given buffered saline. The comparable figures obtained for the JH virus were of 23 (34%) of 69 volunteers given virus and 8 (20%) of 40 concurrent controls. These differences are not statistically significant unless the results obtained with both viruses are combined. 55 volunteers given 2060 or JH virus were challenged 4 weeks to 8 months later with the same or the other virus. Results of these tests indicate that infection by each of these 2 viruses confers immunity against both. On the other hand, no such immunity could be detected among volunteers previously infected with nasal secretions from patients with natural common colds.

JH virus was recovered from 17 volunteers by testing in tissue cultures nasal secretions collected 2 to 6 days after administration of the virus. Positive isolations were obtained from all of 5 specimens from 2 volunteers with colds and from 12 of 42 specimens from volunteers free from symptoms. One of the strains recovered from these volunteers was identified as JH virus by serum neutralization; this same strain was administered to 6 volunteers and produced 2 colds.

4-fold or greater rises in virus neutralizing antibody were detected in all the paired sera available from 9 volunteers from whom virus was isolated. Neutralization titres in the pre-inoculation serum from these volunteers varied from ½ to 1/64. Sera from volunteers given either JH or 2060 virus showed 4-fold or higher antibody rises to 2060 virus in 8 (18%) of 44 pairs to JH virus in 17 (25%) of 68 pairs and to both viruses in 5 (12%) of 41 pairs. Antibody rises were slightly more frequent among volunteers who developed colds (5 of 16) than among those who did not (15 of 55). No antibody rises were detected among volunteers who developed colds in the control groups. [See also TYRRELL and BYNOE, this *Bulletin*, 1959, v. 34, 196.] *H. G. Pereira*

KASEL, J. A., ROWE, W. P. & NEMES, J. L. **Modification of Erythrocyte Receptors by a Factor in Adenovirus Suspensions.** [Correspondence.] *Virology.* New York. 1960, Mar., v. 10, No. 3, 388–91.

VAN DER VEEN, J., OEI, K. G. & PRINS, A. Isolatie van Coe-virus bij patiënten met een acute aandoening van de luchtwegen. [**Isolation of Coe Virus from Patients with Acute Respiratory Disease**] *Nederl. Tijdschr. v. Geneesk.* 1960, Mar. 26, v. 104, No. 13, 617–19.

The English summary appended to the paper is as follows:—

"Virus strains which proved to be immunologically identical with Coe virus were recovered from the throat swabs and stool specimens of three Army recruits suffering from mild respiratory disease. The strains were isolated in fresh cultures of human thyroid cells. The three patients showed a significant rise in neutralizing antibody against the strains recovered from their own throat."

GOFFE, A. P., BEVERIDGE, Jennifer J., MACCALLUM, F. O. & PHIPPS, P. H. **Poliomyelitis Virus in Sewage in 1951.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Jan., v. 19, 9–18, 2 figs. [14 refs.]

A survey of the incidence of polio and Coxsackie viruses in sewage collected from 96 communities in England and Wales in 1951 is presented. MOORE swabs [this

Bulletin, 1949, v. 24, 187] were left in sewers for 3 days once between February and May and again between June and October. 30 sewerage points were selected in each community but a pool of fluids expressed from the swabs was used for virus studies. The treated sewage was inoculated into monkeys and suckling mice. Efforts were made to sample communities with and without a history of poliomyelitis notifications and to sample them at the season of low and of high incidence of poliomyelitis.

Unfortunately, only 4 polioviruses and no Coxsackie viruses were isolated. The incidence of poliomyelitis was very low in 1951 and since only virulent polioviruses would be isolated in monkeys this may partially explain the disappointing isolation results. It seems likely that by means of tissue culture techniques and ultracentrifugation of the samples more isolations could have been made. 3 of the isolations were made from communities where no cases of poliomyelitis occurred. It is noted that during 1951 there were several outbreaks of Bornholm disease due to Coxsackie B3.

[An account of the isolations of bacteria from the same swabs is given by HOLT, 1960, *Ibid*, 1960, v. 35, 536.]

A. J. Beale

FOGH, J., LUND, Rosemary O. & MCCLAIN, Mary E. **Sensitivity of FL Cells to Pclio- and Adenoviruses.** *Arch. f.d. gesamte Virusforschung.* 1960, v. 9, No. 5, 559–70, 2 figs. [28 refs.]

The comparative sensitivity of a line of human amnion cells (FOGH and LUND, *Proc. Soc. Exper. Biol. and Med.*, 1957, v. 94, 532) to polio and adenoviruses is recorded. For poliovirus, with the plaque technique, FL cells were superior to monkey kidney cells, giving both higher titres and lower standard deviations. Similarly the FL cells gave titres 2½-5 times higher for a type 2 poliovirus strain than 3 strains of HeLa cells, Detroit 6 and Chang's conjunctiva cells. Growing FL cells in horse or ox serum instead of human serum impaired their sensitivity. The cells were as satisfactory for propagation of virus as for assay though substantial amounts of virus remained intracellular if virus was harvested just when the cytopathic effect was complete. The behaviour of FL and primary human amnion cells in producing plaques with Lederle chick-embryo-adapted type 2 poliovirus separates them from the other cell lines and monkey kidney cells which did not yield plaques. [The text and Table are at variance on this point.] No satisfatory plaque technique could be evolved for adenovirus, but the FL cells seemed very satisfactory for titrating type 1 at least. It was confirmed that the titre of adenovirus could be determined from the straight line relationship between virus dose and time of onset of a specific degree of cytopathic effect [FOGH, this *Bulletin*, 1956, v. 31, 221]. *A. J. Beale*

LEVINE, S. **The Effect of X-Irradiation on the Yield of Poliovirus.** *Virology.* New York. 1960, Feb., v. 10, No. 2, 257–67. [20 refs.]

The effect of irradiation (1500 r) of host cells on the yield of Leon strain of type 3 poliovirus was investigated. It was found that irradiated HeLa cells were destroyed more quickly than normal cells by poliovirus. The yield of poliovirus from HeLa (S 3 clone) and a continuous line of monkey kidney cells, LLC-MK2 (HULL, *et al. Anat. Record*, 1956, v. 124, 490), was enhanced by X irradiation. Primary monkey kidney cells responded irregularly to irradiation and it was suggested that the failure of cells in primary culture to form giant cells may be the explanation for the general failure to achieve an enhanced yield of poliovirus by means of X-irradiation (see POMERAT, 1958, *Ann. N.Y. Acad. Sci.*, 1958, v. 71, 1143).

A. J. Beale

HÖVEL, H. & SCHNEIDER, W. Struma in der Gewebekultur und ihre Eignung für Arbeiten mit dem Poliomyelitis-Virus. [**The Thyroid in Tissue Culture and its Suitability for Work with Poliomyelitis Virus**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 285–8.

The authors have investigated the use of cultures of adult human thyroid tissue removed at operation as an alternative to monkey kidney cell cultures for the growth of poliomyelitis virus. The thyroid tissue was minced and treated with trypsin; the freed cells were recovered by centrifugation and grown in medium consisting of 0·5% lactalbumin hydrolysate and 5% calf serum in Hank's solution. The cytopathic effect produced by poliomyelitis virus in the thyroid cell cultures resembled that seen in kidney cell cultures. The 3 types of virus could be carried through 7-10 passages in human thyroid cells and the titres attained were of the same order as with monkey kidney cell cultures. *D. J. Bauer*

GROMAN, N., LWOFF, A. & LWOFF, Marguerite, with the technical collaboration of Evelyne RITZ & Marie C. MAIGNÉ. Recherches sur un variant du "froid" du virus de la poliomyélite. [**Studies on "Cold" Variant of Poliovirus**] *Ann. Inst. Pasteur*, 1960, Mar., v. 98, No. 3, 351–9, 4 figs.

A strain of type 1 poliovirus (Brunhilde—Enders—chimpanzee) capable of growing at 25°C. was obtained by passage at progressively lower temperatures. The growth of this strain at various temperatures was investigated. Plaques were produced at 27°C. whereas they were not produced by the parent strain. The cold-adapted strain would still grow quite well at 33 or 35°C. but very poorly at 39°C. or higher temperatures. In parallel with the increase in thermo-sensitivity there was a decrease in neurovirulence.

[The authors have previously reported a more detailed study of the effect of temperature on the growth of polio virus (this *Bulletin*, 1960, v. 35, 617).] *A. J. Beale*

SOKOLOV, M. I., GU, Fan-Chow, SIAO, Dzi-Ho, CHU De-Chun, U, Pin & GO, Chen-Chow. **Enteric Viruses of Man. I. Virological Characteristics of Different Forms of Poliomyelitis in China** *Problems of Virology.* London. 1959, v. 4, No. 2, 53–7. [26 refs.] [Translated from Russian.]

SCHMIDT, Nathalie J., LENNETTE, E. H., HAGENS, Shirley J. & DENNIS, Juanita. **The Behavior of Different Strains of Poliomyelitis Virus in the Complement Fixation Reaction. II. The Sensitivity and Specificity of Antigens derived from Various Strains.** *J. Immunology.* 1960, Feb., v. 84, No. 2, 160–70.

An investigation of the value of several strains of all 3 types of poliovirus as antigens for complement-fixation tests in the diagnosis of poliomyelitis is described. The most comprehensive tests were done with type 1 virus. 9 strains were used to test 35 pairs of sera from patients from whom type 1 poliovirus had been isolated. The differences in titre were slight and there was little to choose between antigens. 3 of the strains, Dennison, Hacker and Kaunert, had previously [SCHMIDT and LENNETTE, this *Bulletin*, 1959, v. 34, 398] been found to be slightly more sensitive than the Mahoney strain in detecting antibodies in the patients from whom the viruses had been isolated. It was found that none of the strains were superior to the Mahoney in this study and that the 2 variant of Brunhilde and the Hacker strain were inferior giving lower titres and smaller rises in antibody titre. A similar study for types 2 and 3 viruses showed that small differences between strains did exist and that the strains routinely employed by the authors, Statler type 2 and McMullen type 3, were satisfactory and that strains do exist that detect lower titres of antibody and a lower proportion of diagnostic titre rises.

In this work a tube complement-fixation test was used with live virus as HeLa cell culture fluid. 16 type 1, 7 type 2 and 12 type 3 poliovirus strains were tested with high titre monkey immune sera and human sera for heterotypic reactions. These did not occur. A few human sera gave titres of 1 in 4 against heterotypic antigens but in the diagnostic test, titres below 1 in 8 are ignored.

A. J. Beale

SPRUNT, Katherine, REDMAN, Winifred M., KOENIG, Susan & ALEXANDER, Hattie E. **Factors influencing Degree of Infectivity of Enterovirus Ribonucleic Acid.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 306–9.

Free RNA obtained from viruses is very much less infective than the original intact virus from which it is derived. Also such free viral RNA is unstable in isotonic solutions but stable in hypertonic ones (*e.g.*, 0·9M NaCl or KCl). It has been suggested that the enzyme ribonuclease is responsible for both stages of RNA destruction, the activity of the enzyme being inhibited in hypertonic salt solutions. In this paper it is shown that RNA derived from type 1 poliovirus is not irreversibly destroyed in isotonic or hypotonic solution. The inactivation is completely reversed by rediluting the RNA in hypertonic salt solutions. This finding means that ribonuclease plays no part in the loss of infectivity of RNA preparations in isotonic diluent. *A. J. Beale*

WENNER, H. A., KAMITSUKA, P., LENAHAN, Margaret & ARCHETTI, I. **The Pathogenesis of Poliomyelitis. Sites of Multiplication of Poliovirus in Cynomolgus Monkeys after Alimentary Infection.** *Arch. f.d. gesamte Virusforschung.* 1960, v. 9, No. 5, 537–58, 1 fig. [14 refs.]

Despite the advances in the study of poliomyelitis, exact knowledge of the pathogenesis of the disease remains fragmentary. The senior author has made extensive efforts to remedy this position, using cynomolgus monkeys. When virus was given intramuscularly, it was found that before the onset of viraemia it could only be found in the muscle inoculated, and in the draining lymph nodes. After viraemia, virus was widely spread but the chief sites of localization were lymph nodes, gastrointestinal tract and central nervous system [this *Bulletin*, 1956, v. 31, 757; 1958, v. 33, 1095]. Now, with a specially invasive type 1 strain of poliovirus (P 1549), investigations have been made of the pathogenesis after alimentary infection.

Virus was given by stomach tube, and the primary sites of multiplication appeared to be the pharynx and, less convincingly, the ileum and in each case the draining lymph nodes. After about 3½ days, viraemia started and lasted 3-5 days. After viraemia, virus was present in all tissue samples but the source of virus maintaining the very high levels in the blood (up to 10^5 TCD50 per ml.) was not certainly determined. Apart from the sites of primary multiplication, virus was found in higher titre than in the blood in lymph nodes, fat (axillary and scapular) and central nervous system. The titre differences in the case of fat and central nervous system tissue were great, but virus did not appear in these tissues till after high levels appeared in the blood. Similarly, lymph nodes were not considered the main secondary site of virus multiplication because again, except for those draining primary sites, they were not affected until after high levels appeared in the blood, and also because the titre differences were slight, suggesting concentration in drainage area rather than multiplication. It is suggested, however, that secondary multiplication occurred in endothelial cells of blood vessels and fixed and wandering mesenchymal cells. This is based on the early appearance of virus in the spleen and bone marrow, the wide dissemination of poliovirus through capillary walls suggesting that these are damaged, and the possibility in this way of explaining the maintenance of high levels of viraemia for about 72 hours in the absence of other recognizable sites of virus multiplication. The route of spread of virus to tertiary target organs such as the central nervous system and brown fat is probably *via* the blood stream. However, virus was frequently found in nerve ganglia before the onset of viraemia and these may have afforded a route to the central nervous system. A striking feature of the results was the great variations between individual monkeys.

[This is a most interesting paper which, however, fails to settle conclusively the problems of the pathogenesis of poliomyelitis.] *A. J. Beale*

SOLOVIEV, V. D. & GENDON, U. Z. **Use of White Rats for the Measurement of Immunogenic Potency of Inactivated Poliomyelitis Vaccine.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 291–3.

"There are many advantages in the use of small laboratory animals rather than primates for tests to determine the immunogenic potency of inactivated poliomyelitis vaccine. The white rat, in particular, is cheap, easy to keep and use in sufficiently large numbers to ensure the statistical validity of results, and highly resistant to intercurrent diseases. The experiments reported show that this animal can be successfully used for evaluating immunogenic potency when a single intraperitoneal inoculation of inactivated poliomyelitis vaccine is administered, with results as accurate as those obtained with the more expensive guinea-pig."

LYCKE, E., LUND, Ebba & HULTGARDH, A. **The Sensitivity of Suckling Mice and Tissue Cultures for Isolation of Coxsackie B Viruses.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 4, 443–8.

During Sepember to December 1958, 16 strains of Coxsackie B virus were isolated in suckling mice, HeLa cells and human embryo lung tissue cultures. 6 of the strains were Coxsackie B1 and 10 B3. All 16 strains were isolated in HeLa cells but 8 of them were only detected after one blind passage in HeLa cells. All but 4 of the tissue culture fluids proved pathogenic for suckling mice, but only 5 of the 16 strains were isolated by direct inoculation of suckling mice; 3 of these 5 isolations were achieved by blind passage in suckling mice. 3 of the strains were isolated in human embryo lung tissue but one of these strains could not be propagated in series. It was thought that part of the reason for the superiority of HeLa cells for detecting Coxsackie B virus might be the larger inoculum used. Normally HeLa cells were inoculated with a 20% faecal suspension. When a 2% suspension was used, only 6 of the 16 strains were detected. In suckling mice, with an inoculum of 0·78 ml. of a 50% suspension instead of 0·42 ml. of a 20% suspension, which is approximately a 5-fold increase in virus dose, no great improvement in virus isolation rate was achieved. One strain that had been isolated originally was not isolated using the higher dose and 2 fresh strains were isolated. *A. J. Beale*

KANTOCH, M. & DUBOWSKA-INGLOT, Anna. **Inhibition of the Phagocytic Activity of Leukocytes by Coxsackie Viruses. II. Serological Studies.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 4, 587–606. [16 refs.]

"The experiments were designed to investigate the effect of Coxsackie viruses, inactivated by specific immune serum, on the phagocytic activity of leukocytes. Coxsackie virus type A4, mouse and guinea pig immune sera, guinea pig leukocytes and two kinds of test bacteria, *E. coli* and *S. aureus*, were used. The degree of the inhibition of phagocytosis was measured by phagocytic index, phagocytic coefficient (PC) according to Davies, and the percentage of phagocytes not containing bacteria (PNCB).

"It was found that Coxsackie virus inactivated by immune serum inhibits the phagocytic activity of leukocytes to the same exent as the active virus. However, the virus thus inactivated causes less extensive morphological changes in leukocytes than active virus. The degree of inhibition of the phagocytic activity of leukocytes by the inactivated virus did not depend on the kind of test bacteria used.

"The experiments, in which viruses inactivated by immune serum were incubated with leukocytes and non-sensitized bacteria were used in the phagocytic test, showed a considerably stronger and quicker inhibition of phagocytosis than that obtained when using active virus. This was due not only to the effect of the virus on leukocytes but also to the interaction between opsonizing factors of fresh serum and the viral antigen-antibody complex.

"The fresh guinea pig serum incubated with the antigen-antibody complex was observed to lose its ability to sensitize *E. coli* and *S. aureus* to phagocytosis. This phenomenon might be due to fixation of the opsonizing constituents of serum by the viral antigen-antibody complex.

"Fixation of the opsonizing substances could be observed as early as one hour after incubation, increasing as the time of contact was prolonged. The degree of fixation depended on the antigen-antibody ratio."

WIGAND, R. Schwierigkeiten bei der Neutralisation von Enteroviren. [**Difficulties with Neutralization of Enteroviruses**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 504–17. [27 refs.]

The English summary appended to the paper is as follows:—

"Difficulties in neutralization tests in monkey kidney tissue culture used for identification of Coxsackie B and ECHO viruses or for demonstration of neutralizing antibodies are sometimes encountered: low serum neutralization titers in early readings and or 'break-through' of the virus in late readings. Individual virus strains exhibit a high or low tendency to break through, which is not dependent on the immune serum. Neutralization titers obtained in early readings are generally more reliable than those of late readings. In cross-neutralization tests with several strains of the same type antigenic differences of the "prime" type and, less frequently, reciprocal antigenic differences are found. Virus strains may be less readily neutralized by their homologous antiserum even in early readings than heterologous strains of the same type. The neutralizability and break-through tendency of a virus strain may be influenced by a mouse passage or by its status of adaptation to the tissue culture. Neutralization may be widely different when different test systems or methods are used. Examples of the various phenomena are demonstrated and some practical conclusions (choice of virus strains for neutralization tests and for preparation of diagnostic antisera, procedure of neutralization tests, etc.) are drawn."

KANTOCH, M. & ZAPF, K. **Electron-Microscopic Studies on the Localization of Coxsackie Viruses in Leukocytes.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 4, 607–13, 8 figs. on 4 pls. [23 refs.]

HAMMON, W. McD., YOHN, D. S. & PAVIA, Rose A. **Isolation and Characterization of Prototype Viruses ECHO-26, ECHO-27, Coxsackie B-6.** *Proc. Soc. Exper. Biol. & Med.* 1960, Jan., v. 103, No. 1, 164–8. [10 refs.]

The Committee on Enteroviruses of the National Foundation now recognizes 3 types of poliovirus, 28 ECHO viruses and 6 Coxsackie B viruses—they have yet to pronounce on the Coxsackie A group. This paper describes the prototype strains of 3 newly recognized enteroviruses, Coxsackie B6, ECHO 26 and 27. All 3 viruses produced cytopathic effects in rhesus monkey kidney cells, but not in HeLa, H.Ep. No. 2, or KB cells, or primary cultures of hamster or cat kidney. They were not inactivated by deoxycholate and did not agglutinate chicken or human Group O red cells. They passed a gradocol membrane 36 millimicrons but not one 28 millimicrons. They did not react in complement-fixation tests with human sera containing adenovirus group antibody. They were all isolated from rectal swabs obtained from healthy people in the Philippines in 1953. The Coxsackie B6 strain (1–51–21) produced typical Coxsackie B type lesions in suckling mice. It killed chick embryos by the yolk sac route but could not be passed serially. It differed from other Coxsackie B strains in lack of effect on several human cell lines. Some strains, but not the prototype, were neutralized by a Coxsackie B1 sera. HUMMELER in Philadelphia has isolated 2 strains from the faeces of children with meningitis.

ECHO 26 (strain 11–3–6) is a distinct serological entity. It produces plaques under agar with low concentrations of bicarbonate (1·25 ml. per 100 ml. of a 7·5% solution of bicarbonate instead of 3 ml.). ECHO 27 (strain 1–36–4) did not produce plaques in monkey kidney cells. It was not pathogenic for suckling mice and formed a distinct serological entity. The antisera to ECHO 27, titre 1:40,000, neutralized Coxsackie B2 at a dilution of 1:20. Human gamma globulin contained antibodies to all 3 viruses as did sera from some individuals in the Philippines. *A. J. Beale*

KALTER, S. S. **Animal "Orphan" Enteroviruses.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 319–37, 3 figs. [Numerous refs.]

"Since the discovery, some ten years ago, of the pathogenic effect of polioviruses on non-nervous-tissue cells, tissue-culture methods have come to be widely used in virological research. Through these improved techniques for studying viruses, a large number of new cytopathogenic agents have been isolated from the intestinal tract of man. Many of these agents have been obtained from persons suffering from polio-like disease, but others have been isolated from apparently normal persons. The term "orphans" is used to designate those viruses which cannot definitely be associated with any recognized disease syndrome.

"The existence of these enteric pathogenic human orphan (ECHO) viruses, and their association with clinical disease in certain cases, stimulated interest in their animal counterparts, which might constitute a serious threat to both human and animal health. In this paper, the author reviews the information at present available on the occurrence of the so-called "orphan" enteroviruses in monkeys, cattle, swine, and other animals in various parts of the world, and discusses the possible interrelationships of these animal viruses with each other and with the human enteroviruses."

KUWATA, T. **Studies on the Infection of Tumor Cells by Extraneous Viruses. II. Susceptibility of Two Transplantable Mouse Tumors to Neurotropic Viruses.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 610–20, 5 figs. [12 refs.]

The author investigated the susceptibility of 2 transplantable mouse tumours, a carcinoma induced by quinone and a sarcoma induced by fructose to infection with certain neurotropic viruses. Mice bearing tumours were infected with Columbia-SK virus on the 8th day after transplantation by injection into the tumour; after 4 days the virus had attained a titre of 10^6 in the tumour and had spread to the brain, where a titre of $10^{6\cdot3}$ was recorded. Similar results were obtained with the sarcoma. Eastern and western equine encephalomyelitis viruses multiplied in the 2 tumours but did not invade the brain. Marked inhibition of growth was observed when the pieces of tumour were treated with Columbia-SK virus before transplantation, but exposure to western equine encephalomyelitis virus had no effect upon the growth rates. Japanese B encephalitis virus multiplied in both tumours to low titres (10^3–$10^{4\cdot8}$) and invaded the brain, but did not effect the growth rate of the tumours. Fixed rabies virus did not multiply in the tumours and had no effect on growth. *D. J. Bauer*

PORTERFIELD, J. S. **A Simple Plaque-Inhibition Test for the Study of Arthropod-Borne Viruses.** *Bull. World Health Organization.* Geneva. 1960, v. 22, Nos. 3/4, 373–80, 3 figs. & 4 pls. [15 refs.]

Monolayers of trypsinized chick embryo cells were grown in tris-buffered media; 8 ml. of 8–10 million cells per ml. were used for a 60 mm. Petri dish [this *Bulletin*, 1959, v. 34, 956; 1960, v. 35, 86; *Trop. Dis. Bull.*, 1960, v. 57, 363]. The cell layers were infected, left for a 2-hour absorption period, then overlaid with agar. Antisera were then applied in "fish-spine" electrical insulating beads which were laid on the agar surface. Antibody diffused through the agar protecting a zone of cells around the bead: for example zones of cells 15 mm. and 20 mm. in diameter were produced by serum of rabbits immunized against yellow fever on plates seeded with 10^{-3} and 10^{-4} dilutions of yellow fever virus. With quick-growing viruses like western equine encephalitis and Semliki Forest a 100-fold change in virus concentration changed the diameter of the zone by only 3–4 mm.—

with slower growing viruses the slope of the relation was steeper: for yellow fever a 100-fold difference in virus made a difference of about 15 mm. in the zone diameter.

When serum dilutions were tested it was found that there was a linear relation between the square of the radius of the zone and the log concentration of serum. Zones decreased in size as the interval between overlaying the cells and applying the fish-spines increased—after 48 hours some effect was demonstrable but none after 72 hours' delay. Zones could be increased in size by incubating the layers with the serum fish-spines on for 24 hours at 30°C. then at 37°C. Thinner overlays increased the zones but the cells survived less well under them. When 5 group A arborviruses were compared in a neutralization test Chikungunya, Mayaro and Semliki showed relationships as did Sindbis with western equine encephalitis. Group B viruses appeared to show even greater specificity. The technique has so far been shown to be applicable to 7 Group A, 4 Group B, and to Bunyamwera, Ilesha and Tahyna viruses. Increased chick embryo extract was found necessary for successful results with louping-ill virus. *C. E. Gordon-Smith*

SANNA, A. & ANGELILLO, B. Protezione crociata tra i virus della Foresta Semliki e Mayaro. [**Cross Protection among Viruses of Semliki and Mayaro Forest**] *Igiene Moderna.* 1959, Sept.–Oct., v. 52, Nos. 9/10, 667–75. [18 refs.]

The English summary appended to the paper is as follows:—

"In a series of researches on cross immunity among ARBOR viruses of the A group, it has been observed that mice previously immunized with Mayaro virus show a significant protection against the virus of the Semliki Forest, of the same group, inoculated through the peripheral route."

SANNA, A. & ANGELILLO, B. Protezione crociata fra i virus della Foresta Semliki e Sindbis. [**Cross Protection among Viruses of Semliki and Sindbis Forest**] *Igiene Moderna.* 1959, Sept.–Oct., v. 52, Nos. 9/10, 676–80.

The English summary appended to the paper is as follows:—

"In agreement with earlier observations by the authors and by Casals with other viruses of the A group, it was found that mice immunized with Sindbis virus show a significant protection against the virus of the Semliki Forest, of the same group, inoculated through the peripheral route."

JETTMAR, H. M. & CRUSE, J. M. Studien über Hämolyse durch Mäusehirnextrakte (mit besonderer Berücksichtigung der Zeckenencephalitis). [**Studies on the Haemolysis produced by Mouse Brain Extracts (with special reference to Tick-Borne Encephalitis)**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Sept., v. 118, No. 3, 195–218. [32 refs.]

Haemolysis of mouse red cells could be produced in low titre by extracts of mouse brain infected with tick borne encephalitis virus and prepared by rubbing with a glass rod in saline followed by 6 cycles of freezing and thawing of the suspension thus obtained. Haemolysis was also produced, but less regularly, by similar extracts of brains infected with encephalomyocarditis, MM, Lansing and vaccinia viruses. After storage at −17°C. for several weeks the brains lost their haemolytic properties, but these could be restored by adding a piece of normal brain devoid of haemolytic activity to the stored brain before preparing the extract. *D. J. Bauer*

ANDONOV, P. S. & SHUBLADZE, A. K. **The Cultivation of Strains of Russian Spring-Summer Encephalitis Group Viruses in Chick Embryo Tissue Cultures and in HeLa Cells.** *Problems of Virology.* London. 1959, v. 4, No. 1, 92–7, 4 figs. [Translated from Russian.]

Skin-muscle from chick embryos was finely minced and grown on the wall of stoppered flasks. Plasma was not necessary for adherence of cells to glass. Although some non-specific degeneration occurred after 8–10 days, cultures could be kept up to 15 days without change of medium. 3 strains of Russian spring-summer virus (Ias–8, Ikh–10, Im) grew in such cultures, the 2 former strains causing a cytopathic effect. Similar results were obtained in HeLa cells. The cytopathic effect was inhibited by immune serum. Chick embryo tissue culture fluids were used as complement-fixing antigen and also to prepare a formolized vacine which was antigenic in mice.

C. E. Gordon Smith

SOKOL, F., LIBÍKOVÁ, H. & ŽEMLA, J. **Properties of Infectious Ribonucleic Acid derived from Brains of Mice infected with Tick-Borne Encephalitis Virus.** *Acta Virologica.* Prague. 1960, Mar., v. 4, No. 2, 65–74, 1 fig. [22 refs.]

The brains of mice infected with the Hypr strain of tick-borne encephalitis virus were extracted in the usual way with phenol and then with ether. The resulting RNA preparations contained 2 x 10^3—7 x 10^4 LD50 per ml. by intracerebral titration in mice—600–40,000 times less than the virus preparation from which they were derived. The RNA was also infective intraperitoneally but not subcutaneously. Treatment with 45 μgm./ml. of ribonuclease at 37°C. for 25 minutes destroyed the infectivity of the RNA but not that of the original virus preparation. Homologous gamma globulin neutralized the original virus 500–13,000-fold but the RNA only 5–7-fold. Normal horse serum inactivated the RNA in 60 minutes at 37°C. 96% ethanol destroyed the infectivity of the original virus but that of the RNA was unaffected. Heating at 37°C. for 4½ hours gave irregular results but in some experiments both the virus and the RNA were reduced about 100-fold in titre. The stability of different RNA preparations at 4°C. varied from 3 to over 72 hours. Virus derived from infections with the RNA was identified by a neutralization test and its pathogenicity was unchanged, as were the histological

appearances in infected mouse brain. The RNA preparations were estimated to contain 276–1,007 μgm./ml. of nucleic acid and to have 4–110 LD50 per μgm. of nucleic acid. *C. E. Gordon Smith*

DANES, L. & BENDA, R. **Study of the possibility of preparing a Vaccine against Tick-Borne Encephalitis, using Tissue Culture Methods. II. The Inactivation by Formaldehyde of the Tick-Borne Encephalitis Virus in Liquids prepared from Tissue Cultures. Immunogenic Properties.** *Acta Virologica.* Prague. 1960, Mar., v. 4, No. 2, 82–93, 5 figs. [18 refs.]

For vaccine preparation the B3 strain of tick-borne encephalitis virus was grown in trypsinized chick embryo cultures. Formalin dilutions from 1:500 to 1:5,000 at 4°C. were compared: inactivation was apparently complete in 24–42 hours at 1:500 and in about 75 hours at 1:2,000 but at lower concentrations active virus remained for 14–20 days. The composition of the tissue culture fluid did not appear to affect the inactivation curves. Centrifugation and filtration through a G3 filter also had no effect; a G5 filter reduced the infectivity and immunogenicity. Variations of the *p*H between 7·2 and 7·5 had no effect. Neutralization of the formalin in the vaccine with $NaHSO_3$ caused re-activation of one of 18 batches of vaccine but did not affect the immunogenicity of the others.

Guineapigs were given 3 doses of 0·5 ml. of vaccines at intervals of 3 to 5 days then bled 10 days later—vaccines inactivated with 1:2,000 formalin gave better neutralizing indices than those with 1:500 or 1:1,000 and this concentration was therefore adhered to. Mice vaccinated with 3 doses and challenged intraperitoneally were protected against 3·2–5·7 LD50. The vaccines were compared with chick embryo and mouse-brain vaccines and some of the tissue culture vaccines were as good although there was considerable variation in potency. The amount of neutralizing antibody and the degree of protection attained in mice depended on the size of the doses administered: 3 doses of 0·01 ml. did not protect significantly; 3 doses of 0·05 ml. protected against 1·0–2·9 log LD50: 3 doses of 0·5 ml. protected against 3·9–>5·8 log LD50. In challenge experiments the vaccine protected mice against 3 strains of tick-borne encephalitis virus, and against louping-ill but very slightly against Kyasanur Forest virus. Preliminary results suggest that the liquid vaccines are stable only for a few months. [These observations can be regarded as preliminary and much remains to be done to demonstrate that this is an acceptable vaccine.]

C. E. Gordon Smith

MCLEAN, D. M. & DONOHUE, W. L. **Powassan Virus: Isolation of Virus from a Fatal Case of Encephalitis.** *Canadian Med. Ass. J.* 1959, May 1, v. 80, No. 9, 708–11, 2 figs. [27 refs.]

A 5-year-old boy at Powassan, Ontario, was admitted to hospital with a history of blinking, tremors and dizziness in September 1958. On admission the temperature was 101°F., there was headache but no neurological signs. The cerebrospinal fluid was normal, but under pressure; the leucocyte count was 15,900 per cmm. An electroencephalogram showed a diffuse abnormal pattern. 2 days later the temperature was 103°F., there was ataxia, neck stiffness and an extensor plantar response. The cerebrospinal fluid now had 150 cells per cmm. (60% lymphocytes). Increasing coma associated with hemiplegia developed and by the fourth day the electroencephalogram was grossly abnormal. Respiration ceased on the fourth day; he remained alive in a respirator only until the 6th day.

At autopsy the brain showed widespread perivascular infiltration and focal parenchymatous infiltration. Newborn mice inoculated with parts of the basal ganglia and cortex were sick 5 days after inoculation, weaned mice 7 days after inoculation. Newborn mice inoculated with cerebellum went down after 7 days, but weaned mice inoculated remained well. Re-isolation was successful. No cytopathic effect was found in monkey kidney cultures and no lesions in chick embryos after inoculation of second mouse passage material. Powassan virus haemagglutinates best at *p*H 6·6 and 4°C. Antisera to St. Louis, Murray Valley, eastern and western equine encephalitis viruses did not neutralize Powassan. Complement-fixation likewise revealed no relationships. Powassan haemagglutinin was however inhibited strongly by St. Louis and weakly by Murray Valley antisera, but not by eastern or western equine antisera. Subsequent study by CASALS [see below] showed Powassan to be a new and distinct member of the Russian spring-summer complex of group B arboviruses. It is the first member of the complex to be isolated in the Americas.

C. E. Gordon Smith

CASALS, J. **Antigenic Relationship between Powassan and Russian Spring-Summer Encephalitis Viruses.** *Canadian Med. Ass. J.* 1960, Feb. 13, v. 82, No. 7, 355–8. [12 refs.]

Powassan virus was isolated from the brain of a child who died of acute encephalitis in Canada and had been shown to have some antigenic relationship to St. Louis and Murray Valley encephalitis viruses. Powassan antigen was therefore tested for complement-fixing activity against antisera to 14 group B arboviruses. Cross-reactions were found only with Russian spring-summer (RSS), Li-32 (RSS group) and St. Louis viruses. With antisera made with only 2 inoculations of antigen differentiation of Powassan from RSS was not difficult: homologous serum titres were 4–8 fold higher than heterologous. In haemagglutinin-inhibition tests Powassan serum cross-reacted with RSS and St. Louis, while Powassan antigen cross-reacted with 7 of 9 group B agents. However, strong cross-reaction was only with RSS. In a neutralization test Powassan serum with a homologous neutralizing index of 1,000 had an index of 60 against RSS and 30 against St. Louis; an RSS serum with a homologous index of 300 had an index of 110 against Powassan; a St. Louis serum with a homologous index of 1,000 had an index of only 8 against Powassan. Powassan thus belongs to the RSS group, but is less closely related than previously known viruses in this

sub-group. This is the first recorded isolation of a virus of this group in the Americas.

Modoc virus, in group B, and isolated from the mammary tissue of a wood mouse in California by H. N. JOHNSON, was included in some of the tests. Modoc is not closely related to the RSS group and appears to be a new, distinct member of group B.

C. E. Gordon Smith

HENDERSON, J. R. & TAYLOR, R. M. **Phlebotomus (Sandfly) Fever Viruses in Tissue Culture.** *Amer. J. Trop. Med. & Hyg.* 1960, Jan., v. 9, No. 1, 32–6, 3 figs. [13 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 699.]

COLLIER, W. A. & DE WIT, M. J. **Adsorption to Ascites Cells and Eclipse Phenomenon of Yellow Fever Virus in Ascites-Carcinoma.** *Trop. & Geograph. Med.* Amsterdam. 1959, Dec., v. 11, No. 4, 339–44, 6 graphs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 698.]

AITKEN, T. H. G. **A Survey of Trinidadian Arthropods for Natural Virus Infections (August, 1953 to December, 1958).** *Mosquito News.* 1960, Mar., v. 20, No. 1, 1–10, 1 fig.

Since August 1953, 800,000 haematophagous arthropods have been processed for virus isolation at the Trinidad Regional Virus Laboratory. 94 strains of virus were isolated from 7,300 pools. Of 84 species of mosquito processed the 6 most common species were *Aëdes serratus, Psorophora ferox, Ps. albipes, Mansonia arribalzagai, Aëdes scapularis* and *Limatus flavisetosus. Wyeomyia* was the genus most often inoculated. Of other arthropods *Culicoides* (6,508) and simuliids (3,238) have been most studied. All the virus isolations were from mosquitoes. 22 of the 24 isolated in adult mice were yellow fever and 2 Ilheus virus. In suckling mice 70 strains representing 14 agents were isolated: 3 are previously known agents—Ilheus, St. Louis and Mayaro viruses—the remainder being apparently new. The viruses isolated and their mosquito hosts are tabulated. The genera suspected of being vectors are *Mansonia, Culex, Aëdes, Psorophora, Trichoprosopon, Limatus, Wyeomyia* and *Phoniomyia.* The most commonly infected species were *Aëdes scapularis, Psorophora ferox* and *Ps. albipes.* [This paper is a condensed summary and contains a wealth of information about the handling, transportation and processing of the various types of arthropod studied.]

C. E. Gordon Smith

CASALS, J. & WHITMAN, L. **A New Antigenic Group of Arthropod-Borne Viruses. The Bunyamwera Group.** *Amer. J. Trop. Med. & Hyg.* 1960, Jan., v. 9, No. 1, 73–7. [11 refs.]

The Bunyamwera group so far includes (1) Bunyamwera, from *Aëdes* spp., Uganda, (2) Wyeomyia, from *Wyeomyia melanocephala,* Colombia, (3) Cache Valley, from *Culiseta inornata,* Utah, U.S.A.; from *Aëdes scapularis,* Belem, Brazil, (4) Kairi, from several genera of mosquitoes, Trinidad; *Aëdes scapularis,* Belem. In neutralization tests, intracerebral tests were more specific than intraperitoneal ones in mice. Haemagglutinins have been prepared only from Bunyamwera and from the Belem strain of Cache Valley virus.

In cross-complement-fixation tests Bunyamwera and Cache Valley cross-reacted strongly with each other but Kairi and Wyeomyia showed little cross-reaction with each other or with the first 2. In intraperitoneal neutralization tests Cache Valley and Wyeomyia antisera neutralized both Bunyamwera and Kairi viruses. The cross-reactions were less in intracerebral tests and Bunyamwera and Cache Valley antisera neutralized their homologous antisera more strongly than the heterologous sera. In haemagglutinin-inhibition tests Bunyamwera antigen was strongly inhibited only by the homologous serum; Cache Valley antigen was strongly inhibited only by antisera to the 2 Cache Valley strains. No cross-reactions were found by any serological method with viruses in groups A, B, and C of arborviruses.

C. E. Gordon Smith

ANDERSON, C. R., AITKEN, T. H. G., SPENCE, L. P. & DOWNS, W. G. **Kairi Virus, a New Virus from Trinidadian Forest Mosquitoes.** *Amer. J. Trop. Med. & Hyg.* 1960, Jan., v. 9, No. 1, 70–72.

10 of 27 virus strains isolated in suckling mice from mosquitoes trapped in August and September, 1955 and 1958, in the Melajo forest in Trinidad were similar and have been named Kairi virus. An eleventh was later recovered near Rio Claro. 4 strains came from pools of *Aëdes scapularis,* 4 from *Wyeomyia* pools (including *W. aporonoma* and *W. ypsipola*), 2 from *Psorophora ferox* and 1 from *Culex spissipes.* After 3 years' storage re-isolation was successful from 5 of 6 of the pools. In early passage the viruses were pathogenic only for baby mice but they were easily adapted to adults in which death occurred after 4–6 days. 3 strains could not be adapted to chick embryos and 1 failed to grow in hamster kidney culture. The identity of the strains with the type strain (Tr 8900) of Kairi virus was demonstrated by cross-neutralization and cross-complement-fixation tests. A potent Kairi complement-fixing antigen failed to react with antisera to 33 other arborviruses. A low titre cross-reaction was found with Bunyamwera antiserum and this virus was subsequently shown to belong to the Bunyamwera group. [See below.]

Only 1 of 63 sera from human beings with prolonged exposure in forest significantly neutralized 631 LD50 of Kairi virus. 2 of 34 howler monkey sera gave partial protection against 741 LD50; 1 of 18 *Cebus* monkey sera completely neutralized the virus. 11 of 19 donkey sera appeared to have neutralizing antibody against 100 LD50.

C. E. Gordon Smith

KOKERNOT, R. H., SMITHBURN, K. C., PATERSON, H. E. & MCINTOSH, B. M. **Isolation of Germiston Virus, a Hitherto Unknown Agent, from Culicine Mosquitoes, and a Report of Infection in Two Laboratory Workers.** *Amer. J. Trop. Med. & Hyg.* 1960, Jan., v. 9, No. 1, 62–9, 1 fig. [18 refs.]

Mosquitoes were trapped coming to bite man at Germiston near Johannesburg. Viruses were isolated from 2 pools: (1) 5 *Culex* (*Culex*) *theileri* and 12 *C.* (*Neoculex*) *rubinotus*; (2) 11 C. (*N.*) *rubinotus*. The first strain made adult mice sick after 4 days and killed in 5–6 days—re-isolation was not attempted. The second was isolated in both adult and suckling mice and re-isolation was achieved. In cross-neutralization tests these 2 strains were shown to be similar and to be less closely related to 2 strains of Bunyamwera virus. Haemagglutinins were prepared by acetone-ether extraction and cross-haemagglutinin-inhibition tests confirmed the similarity of the strains isolated. Antisera to the new strains (Germiston) did not inhibit Bunyamwera antigen but Bunyamwera antiserum did inhibit Germiston antigen. Cross-complement-fixation tests revealed no cross-reaction between Germiston and Bunyamwera and this appears to be the most specific technique for this group of viruses. Cross-challenge also demonstrated this difference.

2 laboratory infections occurred with Germiston virus. One subject had a sudden onset of fever, headache and backache and was off work for 3 days, the other had only transient fever. The former had been infected with Bunyamwera virus 3 years previously and had residual neutralizing but not haemagglutinin-inhibiting antibody at onset. During the course of the illness he showed antibody responses by all 3 serological tests to both Germiston and Bunyamwera viruses. The other patient showed all types of antibody response to Germiston but none to Bunyamwera virus. *C. E. Gordon Smith*

ANDERSON, C. R., SPENCE, L. P., DOWNS, W. G. & AITKEN, T. H. G. **Manzanilla Virus: a New Virus isolated from the Blood of a Howler Monkey in Trinidad, W.I.** *Amer. J. Trop. Med. & Hyg.* 1960, v. 9, No. 1, 78–80.

During investigation of the yellow fever outbreak in Trinidad [*Trop. Dis. Bull.*, 1956, v. 53, 308] in 1954 sera from shot howler monkeys (*Alouatta seniculus insularis*) were inoculated into baby mice. One serum from a monkey shot near Manzanilla yielded a virus which was successfully re-isolated and which did not cross-react in serological tests with any of a large number of other arboviruses. It was shown to be desoxycholate-sensitive [this *Bulletin*, 1958, v. 33, 413]. It was pathogenic for baby mice by either the intracerebral (titres 10^{-5}–10^{-7}) or the intraperitoneal route (titres 10^{-4}–10^{-6}). Viraemia was detected following intraperitoneal but not intracerebral inoculation. It was pathogenic for adult mice by the intracerebral but not the intraperitoneal route. Chick-embryos were highly susceptible: the incubation period by yolk sac inoculations was 3–7 days and 34 passages in eggs were made. Day-old chicks and rabbits were insusceptible and did not develop antibody. Hamsters were susceptible by the intracerebral (incubation period: 5–8 days) but not the intraperitoneal route. Guineapigs were insusceptible but developed antibody. *Cebus* monkeys were insusceptible to both intracerebral and intraperitoneal inoculations. The following mosquito species when inoculated with virus failed to transmit experimentally but virus was demonstrated in them 2–3 weeks after inoculation: *Aëdes scapularis, Aëdes serratus, Culex fatigans.*

None of 47 human sera from forest areas neutralized the virus. 8 of 67 howler monkey sera neutralized the virus after heating at 56°C. for 30 minutes. 6 of these sera were tested for haemagglutination-inhibiting antibody but none was found. *C. E. Gordon Smith*

UNDERWOOD, G. E., with the technical assistance of S. D. WEED. **Studies on Measles Virus in Tissue Culture. I. Growth Rates in Various Cells and Development of Plaque Assay.** *J. Immunology.* 1959, Aug., v. 83, No. 2, 198–205, 2 figs. [21 refs.]

The Edmonston strain of measles virus has been grown in cultures of human amnion, monkey kidney and HeLa cells. In cultures of HeLa cells mixed with virus in a multiplicity of 10 before seeding titres of 10^5–10^6 TCD50 per ml. were attained after 5 days. Good yields of virus could be obtained with much lower multiplicities, provided that the harvest was made when the cytopathic effect had reached its maximum extent. Incubation at 32°–33·5°C. gave titres which were 0·5–1 log unit higher than those obtained at 37°C. Plaques could be obtained on HeLa cell monolayers with a plasma overlay, and a study of the adsorption of measles virus on to HeLa cells carried out by plaque counting showed that 4 hours were required for practically complete adsorption.

D. J. Bauer

CARLSTRÖM, G. **Comparative Studies on Measles and Distemper Viruses in Suckling Mice.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 527–38. [19 refs.]

Measles virus from human embryo kidney tissue cultures has been carried through 30 intracerebral passages in mice aged 12–24 hours. The virus attained a titre of 2 log units in the brain, and its identity was confirmed by neutralization tests in infant mice with specific antisera. After adaptation to mice the virus could no longer be passaged with certainty in human embryo kidney cultures. The antigenic relationship between measles and distemper was investigated in cross-neutralization tests in mice carried out with mouse-adapted strains of the 2 viruses. An antigenic ratio of 0·2 was obtained, indicating that the viruses were antigenically distinct.

D. J. Bauer

CARLSTRÖM, G. **Correlation between Canine Distemper and Measles Virus neutralizing Capacities in Human Sera.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 539–48. [12 refs.]

Paired acute- and convalescent-phase sera from 14 patients who suffered from measles during an epidemic

in Stockholm in 1957 were examined for the presence of antibody to measles and canine distemper viruses by means of neutralization tests in infant mice with mouse-adapted strains of the 2 viruses. A significant rise in titre of measles neutralizing antibody was observed in all patients, and a significant rise in distemper neutralizing antibody in 10 patients. The ratio of titres of distemper and measles antibodies ranged from 1/125 to 1/5. A similar correlation between the presence of the 2 antibodies was found in the sera of 14 children who had been found to possess distemper antibody in a previous investigation, and distemper-neutralizing antibody was found in 5 of 6 sera from children living in Iceland, where distemper has not occurred for the past 12 years. It is concluded that measles is mainly responsible for the presence of distemper-neutralizing antibody in human sera. *D. J. Bauer*

LOZOVSKAIA, L. S. **Destructive Action of Light on Measles and Influenza Viruses during Desiccation and Subsequent Storage** *in vacuo*. *Problems of Virology*. London. 1959, v. 4, No. 1, 56–9. [Translated from Russian.]

"In the process of drying measles virus a considerable proportion is destroyed if the material is not protected against the effect of diffused day or artificial light. Under the influence of light the titre of the PR_8 strain of influenza virus also fell on drying for 44 hr. It was also ascertained that light exerts a destructive action on dried (residual moisture 0·8–1·5%) preparations of measles and influenza viruses."

TRAUB, E., with the technical assistance of F. KESTING. Über die natürliche Übertragungsweise des Virus der lymphocytären Choriomeningitis (LCM) bei Mäusen und ihre Parallelen zum Übertragungsmodus gewisser muriner Krebsviren. [**On the Natural Mode of Transmission of Lymphocytic Choriomeningitis (LCM) Virus in Mice with reference to its Similarity to that of certain Murine Cancer Viruses**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 4, 453–71. [26 refs.]

The English summary appended to the paper is as follows:—

"The capacity of wild house mice (mus musculus) to infect white mice with LCM virus by contact decreased progressively during a period of 9 months. Antibodies did not seem to be responsible for this change.

"White mice infected by contact or by inoculation early in pregnancy frequently transmitted the virus to part of their embryos, the percentage of infected embryos varying between 10 and 100%. There was no clear correlation between the relative number of infected embryos and the time elapsing between infection of the mother and parturition. There is good evidence for transplacental infection of the embryos in these cases.

"In contrast to this, the embryos of numerous viru carriers were all infected at an early stage of develop ment. The infection evidently occurred in the oval state This mode of infection is designated as congenital (since transovarian infection has not yet been proved), th former as transplacental.

"Congenitally infected females regularly transmitte the virus to their embryos in successive pregnancies i contrast to pregnant mice infected by contact. However some of the latter animals lost their immunity in th course of 2 to 3 months and then again produced infecte litters when mated with infected males.

"The milk of congenitally infected females prove infectious for suckling mice which became carriers an frequently acquired an immunological tolerance toward LCM virus. Adult mice infected experimentally did no transmit the virus to normal sucklings either with th milk or by contact even when they had just delivere infected litters.

"The epidemiological similarities between LCM an certain murine tumor viruses are briefly discussed."

TRAUB, E., with the technical assistance of F. KESTING Über die immunologische Toleranz bei der lympho cytären Choriomeningitis der Mäuse. [**Immuno logical Tolerance to Lymphocytic Choriomenin gitis in Mice**] *Zent. f. Bakt.* I. Abt. Orig. 1960 v. 177, No. 4, 472–87. [22 refs.]

The English summary appended to the paper is a follows:—

"Mice infected in utero with LCM virus failed t produce complement-fixing and neutralizing antibodie when hyperimmunized later in life. They were immuno logically tolerant. In contrast to them, the complement fixation titer of the serum of non-tolerant adult mic increased considerably as a result of hyperimmunizatio

"Neutralizing antibodies could not be detecte regularly even in the sera of hyperimmune non-toleran mice. Their significance as an immunity factor of prim importance remains problematic. There was also n correlation between the amount of complement-fixin antibody in the serum and cerebral immunity.

"Neonatal infection did not regularly cause immuno logical tolerance. The ratio of tolerant and non-toleran mice decreased rapidly with increasing age at the tim of infection. It was zero in animals 8 days old or olde Intracerebral inoculation of virus produced toleranc more frequently than intranasal instillation or infectio through the milk.

"Different strains of LCM virus were differentl pathogenic following intracerebral inoculation in new born mice. The non-pathogenicity of some strains i such animals cannot be attributed to immunologica tolerance.

"A relationship seems to exist between the appearanc of characteristic convulsions and antibody formation i suckling mice."

IMMUNITY

BOYDEN, S. V. **Antibody Production.** *Nature.* 1960, Mar. 12, v. 185, 724–7, 1 fig. [27 refs.]

This hypothesis on antibody production qualifies for inclusion in the category of "elective" rather than "instructive" antibody theories. Speculating from a phylogenetic point of view, the author discusses the specific immune response of higher animals, assuming that its mechanisms are basically similar to, and in fact evolved from, those which are responsible for the ability of invertebrate phagocytic cells to recognize and respond to foreign matter. He envisages the specialized antibody-forming cells as being coated with "receptors" for a wide range of foreign molecules (antigens), these "receptors" being closely related to, if not identical with, gamma globulins. It is assumed that the antigen, after combining with the "antigen-receptor", enters the cell and becomes fixed in such a way as to be protected from enzymatic break-down. The complex (antigen plus cell component) now interferes with a gamma-globulin cycle of synthesis and breakdown; the intracellular accumulation of gamma-globulin molecules possessing an affinity for the antigen, "modifies" the cell so that more antigen is taken up; cell division is stimulated and so a "clone" of "modified" antibody-forming cells is built up. The hypothesis resembles the "clonal selection theory" of BURNET [this *Bulletin,* 1959, v. 34, 1310] in that it postulates a selection of certain cells, but it is a selection of cells which have been modified as a result of contact with antigen, and not, as in the clonal theory, a selection of genetic variants. *D. A. Cannon*

VAUGHAN, J. H., DUTTON, Anne H., DUTTON, R. W., GEORGE, Mariam & MARSTON, R. Q. **A Study of Antibody Production** *in Vitro.* *J. Immunology.* 1960, Mar., v. 84, No. 3, 258–67, 6 figs. [21 refs.]

DUTTON, R. W., DUTTON, Anne H., GEORGE, Mariam, MARSTON, R. Q. & VAUGHAN, J. H. **Phosphate Metabolism of Spleen Cells in Antibody Formation.** *J. Immunology.* 1960, Mar., v. 84, No. 3, 268–72, 1 fig. [12 refs.]

NETER, E., RAJNOVICH, E. & GORZYNSKI, E. A. **Study of Staphylococcal Antibodies of the Rantz Type: Placental Transfer and Titers in Sera of Children of Various Ages.** *Pediatrics.* Springfield, Ill. 1960, Jan., v. 25, No. 1, 21–6. [19 refs.]

The basic haemagglutination test and its enzyme (protease) modification [this *Bulletin,* 1960, v. 35, 178] are used to detect antibodies to the NSS antigen of RANTZ [*ibid.,* 1956, v. 31, 1278] in maternal and cord blood and sera of children. This antigen can be extracted by phenol from staphylococci, streptococci of groups A, C and G. *viridans* type streptococci, pneumococci, enterococci and *Bacillus subtilis.*

Antibodies to this antigen were present in 40 of 42 maternal sera and 37 cord bloods from babies of these mothers. Only 21 of these cord specimens contained antibodies to *Escherichia coli* 055 although it was present in all maternal sera. The enzyme test was more sensitive than the basic haemagglutination test. 62% titres to Rantz antibody in cord sera were identical or only two-fold lower than in the maternal sera, while titres of *E. coli* antibody were significantly lower in cord than maternal sera. These findings indicate that the Rantz antibody passes the placenta efficiently.

A study of Rantz antibody titres in 185 children of various ages showed significant titres in 94% of infants. At 6–10 weeks this was decreased to 23%, and rose to 73% in children of 2–6 years. All children over 6 years had this antibody.

The authors point out that the enzyme haemagglutination test is more sensitive than the basic test and that this may be because the modified test detects incomplete and complete antibody while the basic test detects only the latter. *M. Patricia Jevons*

GREENBAUM, D. S. & MILLER, L. **Antibody in Milk and its Role in Passive Immunization.** *J. Lab. & Clin. Med.* 1960, Feb., v. 55, No. 2, 229–44, 2 figs. [30 refs.]

The authors tested the hypothesis of PETERSEN and his co-workers (*Science,* 1957, v. 125, 932; *J. Dairy, Sc.,* 1958, v. 41, 726) that the bovine udder responds to the injection of certain antigens in the teat canal by the secretion of a high concentration of specific antibodies directly into the milk. Using diphtheria fluid toxoid, they compared the diphtheria antitoxin concentration in the milk and blood of 2 groups of cows, 1 group immunized by udder infusion, and the other by subcutaneous injection. In contrast to the results of Petersen, the blood was found to have a consistently higher level of antibodies than the milk, suggesting that the antibodies in milk represent a "spill-over" from the blood rather than specific formation in the udder with reflux into the blood stream. The milk titre averaged 3% of the blood titre. The *Salmonella* agglutinin titre, in cows injected with *Salmonella pullorum* vaccine, averaged 8% of the blood titre.

Acute unilateral mastitis was induced with intramammary *Salmonella pullorum* vaccine in a cow which had been immunized with both antigens. The abrupt rise in antibodies in the milk which followed, was temporary for diphtheria antitoxin and persistent for *Salmonella* agglutinins: acute mastitis seemed to increase the permeability of the udder to antibodies.

Regarding the possibility of passive immunization by drinking antibody-rich milk, 3 human subjects with low diphtheria antitoxin titres ingested large doses of equine diphtheria antitoxin mixed with skim milk. In one subject antitoxin was also injected through a tube into the jejunum. In no instance was there a detectable increase in blood titres. Insufficient absorption of antitoxin seemed the most likely explanation. *D. A. Cannon*

ISACSON, P. **Cellular Transfer of Antibody Production from Adult to Embryo in Domestic Fowls.** *Yale J. Biol. & Med.* 1959, Dec., v. 32, No. 3, 209–28, 9 figs. (6 on 3 pls.) [10 refs.]

The ability of adult reticulo-endothelial cells to colonize a recipient and to produce injurious antibodies against the antigens of the recipient has been postulated

and called the "donor v. host" reaction. When adult fowl spleen cells were inoculated intravenously into chick embryos, the spleens of the recipient embryos became massively enlarged, the enlargement bearing an inverse relationship to the age of the embryo. In the youngest embryos large foci of mononuclear cells appeared in the spleen and passed through stages of proliferation, reaction, cell destruction and finally complete necrosis. This sequence of events could also be demonstrated by the inoculation of leucocytes from the peripheral blood. Only slight splenic enlargement occurred when cells were transferred between antigenically similar inbred strains. It appeared that the number of donor cells required to initiate splenic enlargement was too small to be entirely consistent with all aspects of BURNET'S "clonal selection" hypothesis [this *Bulletin*, 1959, v. 34, 1310].

When the donor fowl had been previously immunized with heat-killed influenza virus, the transfer of spleen cells to embryos resulted in the appearance of anti-haemagglutinating antibodies in the sera of the younger recipients. An attempt to initiate antibody production when the adult fowl spleen cells had previously been mixed with virus *in vitro* was not successful, possibly because of the nature of the antigen or a lack of sensitivity in the test system.

Passage of the spleens of embryos showing high titres of antibodies into further groups of embryos resulted in the transfer of splenic enlargement and focal cellular proliferation through several passages but the ability to produce specific antibodies was lost after the first passage.

Whether the implantation of adult cells in a recipient spleen stimulates reproduction and antibody formation, or whether the whole phenomenon represents inductive changes in the recipient spleen, is fully discussed; possibly both mechanisms are involved. *D. A. Cannon*

TALIAFERRO, W. H., TALIAFERRO, Lucy G. & PIZZI, Aida K. **Avidity and Intercellular Transfer of Hemolysin.** *J. Infect. Dis.* 1959, Nov.–Dec., v. 105, No. 3, 197–221, 9 figs. [25 refs.]

The authors described an elegant method for measuring the intercellular transfer of the large Forssman haemolysin from sensitized sheep red cells to unsensitized sheep red cells whose haemoglobin was labelled with ^{51}Cr. Percentage transfer was obtained in terms of the number of 50% haemolysin units which had to be adsorbed on to the carrier cells to result in the transfer of one 50% unit to the ^{51}Cr-labelled cells.

There was a roughly inverse relationship between percentage transfer and haemolysin titre for any given serum whether normal or immune. Normal sera showed high percentage transfer as compared with immune sera. During primary response the percentage transfer fell sharply to reach a minimum value coincident with maximum haemolysin titre and then slowly increased as the titre declined. Similar changes occurred during the anamnestic response, the percentage transfer reaching a lower minimum than during primary response.

Both normal and immune rabbit sera contained a non-avid and an avid component, the latter increasing after immunization to a greater extent than the former.

John R. Norris

OSAWA, E. & MUSCHEL, L. H. **The Bactericidal Acti of Normal Serum and the Properdin Syste** *J. Immunology.* 1960, Feb., v. 84, No. 2, 203– [27 refs.]

"The bactericidal action of normal serum was fou to require the presence of a substance which may regarded as antibody. In the absence of antibody, nor serum was lacking in bactericidal action despite presence of the properdin system. In the presence antibody, properdin may augment the bactericidal t of normal serum to a slight degree. Moreover, bactericidal action of properdin is extremely slight co pared to antibody and is difficult to demonstrate. Fina the experimental findings leading to the concept t homologous antibody may interfere with bacterici action of normal serum attributed to properdin were confirmed."

[Reference should be made to the original paper details of the experimental work and appreciation the excellent long discussion.]

AMANO, T., FUJIKAWA, K., MORIOKA, T., MIYAMA, & ICHIKAWA, S. **Quantitative Studies on Immu Bacteriolysis. I. A New Method of Quantitat Estimation.** *Biken's J.* Osaka. 1958, Nov., v. No. 1, 13–25, 6 figs. [12 refs.]

"A new method has been designed for the quantitat determination of immune bacteriolysis *in vitro*.

"After incubation of the assay tubes containing a serum, complement and a cell suspension of *Escheric coli*, 0·05% final concentration of Na-desoxycholate added to the tubes. By this procedure only ser spheroplasts formed by the immune bacteriolysis destroyed. After centrifugation of the lysates the sup natants are deproteinized with perchloric acid at a fi concentration of 2%, and recentrifuged. Ultravio absorption of these centrifuged supernatants is estima in a Beckman spectrophotometer at 260 mμ. Thus amount of nucleic acid involved in lysates is determin

"By this method, 50% bacteriolytic units of comp ment could be estimated and the course of immu bacteriolysis was studied quantitatively."

LANDY, M., TRAPANI, R. J. & ROSEN, F. S. **Inacti tion of Endotoxin by a Humoral Compone VI. Two Separate Systems Required for Via and Killed** *Salmonella typhosa. J. Clin. Inve gation.* 1960, Feb., v. 39, No. 2, 352–63, 1 [15 refs.]

This is a further paper dealing with the endotox detoxifying component discovered by the authors in blood of mammalian species and identified by attribu which distinguish it from other substances in blood known biological activity [this *Bulletin*, 1959, v. 34, 2 It records the results of experiments which show th by appropriate interaction *in vitro* with serum, it possible to eliminate characteristic host-reactive prop ties of a typical gram-negative species.

The following summary is appended:—

"Alteration of the endotoxin of *Salmonella typhosa* in its native state on the bacterial surface, after incubation with serum, was studied. Changes in endotoxic behaviour were measured by the loss of two characteristic attributes; *viz.*, induction of hemorrhagic necrosis in mouse Sarcoma 37, and stimulation of specific antibody formation in rabbits. The endotoxic activity of typhoid bacilli killed by heat or by chemical treatment was inactivated by endotoxin-detoxifying component (EDC), the same agent previously shown to affect isolated endotoxin, but was not inactivated by antibody and complement. In contrast, the endotoxic activity of viable bacilli was not affected by EDC but was eliminated by antibody and complement, the recognized bactericidal system of normal serum. Viability was thus the critical factor in determining which of these two humoral systems exerted an effect on the endotoxin of typhoid bacilli" *D. A. Cannon*

MAKARI, J. G. **An Antibody Inhibitor.** *Nature.* 1960, Mar. 12, v. 185, 747–9.

It is many years since the author described an "inhibitor" which had the capacity of inhibiting the flocculation of normal globulins in the presence of cephalin cholesterol emulsion. He now adduces evidence that this inhibiting factor is also an antibody inhibitor, capable of preventing the fixation of antibodies to guinea-pig uterine segments in the Schultz-Dale test. In some stages of cancer, he claims, the inhibiting factor is capable of inhibiting antibodies associated with certain serum fractions; at other stages it is not. There appears in cancer to be an immunological defect in antibodies found in certain serum fractions, and also a defect in the inhibiting factor itself found in cancer sera. The author believes that this new concept of an antibody inhibitor will be of assistance in allergic diseases, auto-immune disease and the ageing process, as well as in cancer. *D. A. Cannon*

MARCUS, D. M. **A Study of the Mechanism of the Anticomplementary Activity of γ-Globulin.** *J. Immunology.* 1960, Mar., v. 84, No. 3, 273–84, 1 fig. [36 refs.]

LUZZIO, A. J. **Effects of X Rays on Antibodies.** *J. Infect. Dis.* 1960, Jan.–Feb., v. 106, No. 1, 87–90. [10 refs.]

Continuing his work on the selective effects produced by X-rays on haemagglutinins [this *Bulletin*, 1959, v. 34, 41], the author sets out to determine the relative radio-sensitivities of bacterial agglutinins. Using 4 strains of *Salmonella* and a *Proteus* $X11_2$ he studied the results of exposing the agglutinins, in rabbit immune sera, to the same dose of ionizing radiation. Some specific combining groups were inactivated; others were relatively unaffected. This supported the hypothesis that various antibody-combining sites possess specific radio-sensitivities, and that antibodies may be removed selectively from a polyvalent serum. It is suggested that the denaturation of antibody proteins by ionizing radiation proceeds in an orderly sequence of events, which raises the possibility of inactivating certain unwanted cross-reacting agglutinins while retaining full benefit of others. *D. A. Cannon*

i. VOISIN, C., MARTIN, G. & AERTS, C. Action du virus grippal sur l'activité des leucocytes de l'exsudat péritonéal provoqué chez le cobaye. Étude microcinématographique en contraste de phase. [**Action of Influenza Virus on the Activity of Leucocytes in Artificially Produced Peritoneal Exudate in Guineapigs. Microcinematographic Studies with Phase Contrast**] *Ann. Inst. Pasteur de Lille.* 1958–1959, v. 10, 201–10, 9 figs. on pl. [29 refs.]

ii. ——, —— & ——. Étude du comportement leucocytaire après phagocytose mixte de particules minérales (charbon, quartz) et infectieuses (virus grippal). Étude microcinématographique en contraste de phase. [**Study of Leucocyte Behaviour After Mixed Phagocytosis with Carbon and Quartz Particles and Influenza Virus**] *Ibid.*, 211–18, 9 figs. on pl. [11 refs.]

The English summaries appended to the papers are as follows:—

i. "The microcinematographic observation of the guineapig leucocytes subjected *in vivo* to the action of various strains of influenzal virus discloses intense alteration in cells: bulky appearance, decrease in the number of specific granulations, tendency to vacuolisation, inhibition of migration.

"This cellular attack, most prominent with the B Lee stock, is no longer observed when the influenza-virus has previously been heated for half an hour to 56°C., so as to suppress its infective power together with its toxicity. In the guineapig an animal refractory to influenzal infection, the cellular injuries which we have noticed appear to be related to the toxicity of the viral particles."

ii. "The phagocytosis of coal-particles does not alter the behaviour of the leucocytes of the peritoneal exudate provoked in the guineapig. On the other hand, quartz slows the movement of the cells and causes large vacuoles to appear.

"The phagocytosis of a mixture of quartz, coal and virus particles results in extensive morphological and kinetic changes, of the type observed under the influence of the virus alone.

"The inactivation of virus activity by heat prevents these lesions from appearing and leaves only those observed under the influence of quartz."

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. No. 179. **Requirements for Biological Substances. 3. Requirements for Yellow Fever Vaccine. 4. Requirements for Cholera Vaccine. Report of a Study Group. Geneva, 1–6 September 1958.** 46 pp. [Refs. in footnotes.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

[An abstract of this paper appeared in the *Tropical Disease Bulletin*, 1960, v. 57, 699.]

Miscellaneous

VALENTINE, J. **Old Witch Doctors Never Die. The Inyanga Problem in South Africa.** *New Zealand Med. J.* 1959, Dec., v. 58, No. 328, 791–4.

There are 2 groups of medicine men in South Africa, the herbalists and the diviners (or spiritualists), but to some extent each practises the other's art. They are given special training by older practitioners, and they have considerable traditional knowledge of remedies of various kinds, but they also use antibiotics, having observed their value. The strongest medicines are thought by some to be those made from parts of the human body, especially from persons specially selected and killed for the purpose, and in particular from unborn children.

Witch doctors are of course greatly feared, as possessing supernatural powers, and it is therefore exceedingly difficult to obtain evidence of their more serious activities, for the people will not talk to Europeans attempting to investigate murders possibly connected with their medicines. The author thinks that the influence of witch doctors is increasing, and that they are adapting the powers of modern medicine, and of religion, to their own use.

[It is evidently unwise to forget that beliefs which resemble those current in Europe only a few centuries ago, are still extremely potent in many parts of the world.] *Charles Wilcocks*

FOSTER, F. H. **Domestic Accidents.** *New Zealand Med. J.* 1960, Jan., v. 59, No. 329, 50–54.

This is an account of the results of a statistical survey of domestic accident patients admitted to New Zealand public hospitals in 1957. The magnitude of the accid problem is indicated by the fact that the aggregate ti spent in hospital by domestic accident patients approximately 5% of the aggregate stay for all patie in the hospitals.

There is a detailed description of the accident patie in terms of age and sex with 7 tables in which the cau of accident are summarized under the headings: ac dental poisonings; falls; machinery accidents; sha objects; burns and scalds; foreign bodies and oth accidents.

The total number of accidents was 8,323. There we 845 cases (483 male and 362 female) of poisoning. Dru particularly barbiturates, aspirin and salicylates account for 42·4% of the total. Of the cases of poisoning other substances nearly four-fifths were in children ag 2 years and under. Kerosene was a frequent cause a nearly all the cases of poisoning by this substance we in children aged 2 years and under.

Falls in and about the home were the most freque cause of accident. There were 3,371 cases of whi 1,966 were in females. Analysis of these female cas of accidental falls showed that the aggregate length stay in hospital of these female patients was exceed only by those admitted for each of the 4 groups diseases—respiratory tuberculosis, malignant disea vascular lesions of the central nervous system and co plications of pregnancy and childbirth.

There is a considerable description of the differe kinds of accident which may occur in each group causes with emphasis on the fact that a real saving domestic accidents could be prevented.

M. E. Delafield

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